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THE AMERICAN
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VOL. 101 AUGUST, 1929 No. 8

EDITORIAL

PHARMACOPŒIAL POLICIES

ELSEWHERE in this issue there is printed a timely article by Professor E. Fullerton Cook, Chairman of the Committee of Revision of the United States Pharmacopœia. It enumerates and explains the twelve cardinal points in pharmacopœial policy. Chairman Cook is well qualified to pick these points of policy. His familiarity with revision technic dates back to his association with Remington, the greater part of whose useful life was spent in pharmacopœial service. Almost a decade has passed since the last Pharmacopœial Convention met in Washington (1920). The duties entrusted by that convention to its Revision Committee have been promptly and ably performed. The current Pharmacopœia, known the world over as the outstanding book of medicinal standards is a tribute to the intelligence and industry of that great group of workers constituting the Revision Committee. Quoted from *International Clinics* the following paragraph affords a very fair estimate of the work turned out by this committee, and the great credit which came to pharmacy through its medium:

> "I have before me as I write the last revisions of the United States Pharmacopœia and of the National Formulary. Here are master works of medicinal standards, works accepted the world over as the finest of their kind. Here are the legal instruments whereby the government of the greatest Republic in the world regulates the standards of manufacture and dispensing of medicinals within its boundaries. Here are the mechanisms whereby drug importations are controlled. Here are the authorities whereby drugs are made safe for democracy, and here are standards that provide the means whereby a potent tincture in Kalamazoo is no less and no more potent than the same galenical in Tompkins' Corner.

"And organized American pharmacy is eighty per cent. responsible for the high character of these world known books of standards. This performance alone, to our mind, entitles pharmacy to recognition as a profession of high caliber."

And so do we respectfully urge those who have an abiding interest in the future welfare of Pharmacy to read carefully the aforementioned article.

For only with a correct understanding of these points of policy will it be possible for Pharmacy to be worthily represented in the work of the Convention, which will shortly meet, and in the work, too, of the Revision Committee which will be responsible for the character and caliber of the Eleventh Decennial Revision of the Pharmacopœia of the United States.

IVOR GRIFFITH.

ORIGINAL ARTICLES

ILLICIUM RELIGIOSUM, SIEBOLD*

Mang Tsao

A PHYTOCHEMICAL STUDY

By Sze Yee Chen

(*To be Continued in the September Issue*)

Introduction

ILLICIUM RELIGIOSUM, Siebold, *Mang Tsao* in Chinese, *Shikimi no ki* in Japanese, or commonly known as Japanese star anise, is a plant belonging to the family *Magnoliaceae* and is generally considered by the Chinese and the Japanese, and indeed from the earliest times, to be a poisonous plant. It is directed not to be used internally nor to be applied to the eye.[1] Since the fruit resembles that of the true star anise, *Illicium verum,* Hooker, so closely that it is often mistaken for the latter, or sold as adulterant, many cases of poisoning have been attributed to this plant, especially to its fruit. In

*Thesis submitted for the degree of Doctor of Philosophy, University of Wisconsin, 1927.

[1] Li Shih-Cheng, *Pentaso Kang Mu,* 1596 A. D., chap. 17.

1880, death due to intoxication occurred at Leeuwarden, in the Netherlands, through the use of commercial star anise in the preparation of anise milk which was usually made of oil of anise. According to a report of the commission at Leeuwarden which was charged with the investigation of the poisoning case and which was supplemented by a committee of Amsterdam,[2] Japanese star anise is said to have been used in the preparation. Since that time many cases of poisoning have been recorded by Eykman,[3] by Langgaard,[4] in the *Journal de Pharmacie et Chimie*,[5] by Inoko,[6] in the New York Med Jour.,[7] by Mense,[8] by Guerrero, Paz and Guerrero,[9] by Read,[10] and others.

The morphological description and the anatomical structure of this drug have been worked out at length, yet the chemical investigation is still in a very imperfect stage. The present study deals with the dry fruit and consists of a preliminary analysis, an investigation of the fatty and volatile oils, a study of the shikimic acid which it contains, and the attempted isolation of the toxic principle.

History of Name. *Illicium religiosum*, Sieb. is commonly known in Chinese as *mangtsao* and as *shikimi* in Japan. During his travel in Japan in 1690-1692, Kaempfer [1] fully described this tree under the names *Somo, Shihim, Fanna shikimi, Fanna skiba,* and *Fanna.* Linné first designated the plant as *Badianifera anisata* later as *Illicium anisata* [2] and finally as *Illicium anisatum*,[3] and thought the tree described in Kaempfer's *amoenitates* as the mother plant of the star anise on the market. Loureiro [4] in 1790 first noticed the differences between the Chinese and the Japanese star anise. Siebold [5] in 1827 differentiated the two fruits by the poisonous action of the shikimi

[2] *Pharm. Weekbl.* 17 (1880), No. 4; *Pharm. Jour.* 40, p. 1067.

[3] *Pharm. Jour.* 40 (1881), p. 1046.

[4] *Virchow's Archiv* 86 (1881), p. 222.

[5] *J. de Pharm. et de Chim.* (Editorial) 118 (1884), p. 367.

[6] *Chiugai Iji Shipo* (*Medical News of the World*), Tokyo (1890), pp. 1245-1248 and 1317-1320.

[7] Editorial, vol. 23 (1901), p. 642.

[8] *Handb. der Tropenkrankheiten*, 2d ed. (1914), vol. 2, p. 549.

[9] *Philippine Jour. Sc.* 11-B (1916), p. 203.

[10] *China Med. Jour.* 36 (1922), p. 303.

[1] *Amoenitates exoticarum*, 1712, p. 880.

[2] *Sp. pl.*, 1764, p. 664.

[3] *Systema naturae*, 1825, p. 643.

[4] *Flora Cochinchinensis* (1790), I, p. 353.

[5] *Synopsis plant. oeconom. regn. Japon.*; Tschirch, *Handb. d. Pharmakog.* II, 2 (1915), p. 1215.

fruit and renamed the tree as *Illicium Japonicum* which was accepted in the *Flora Japonica* (1835) by Siebold and Zuccharini.[6] This name was again changed into *Illicium religiosum* in 1837 by Vriese, since it is planted on graves or near temples and used in religious ceremony.[7]

In order to avoid confusion in using the term *Illicium anisatum*, Hooker [8] designated the tree of the true star anise by *Illicium verum* in 1888.

Synonyms. Besides *Mang Tsao* in Chinese and *Shikimi* in Japanese, *Illicium religiosum* is also known by many other names. Since very frequently the Chinese and Japanese names are written in the same characters it is hard to tell their ultimate origin. The following synonyms are, therefore, grouped according to the language in which they appear.

Description of the plant. Illicium religiosum has been fully described by Li Shih-Cheng in *Peng Tsao Kang Mu* (1596) chapter 17 under the name *Mangtsao;* by Kaempfer in his *Amoenitatum* (1712) p. 880, under the name *Somo, Shikimi* etc.; by Loureiro in the *Flora Cochinchinensis* (1790), p. 353 under the name *Illicium anisatum;* and by Siebold in the *Flora Japonica* (1871), p. 5, under the name *Illicium Japonicum.* Holmes [1] Eykman [2] Tambon [3] Ihoko [4] and others have reported additional information.

The plant is about 6 to 20 feet high. The bark has an aromatic odor and a gray color. The leaves resemble those of the laurus or bay tree. They are shortly (about 1 cm.) petioled, coriaceous, thick, feel waxy to the touch, are evergreen, oblong or oblong obovate, acuminate, cuneate at the base, entire at the margins, free from hairs, about 7 cm. long, 3-4 cm. broad and have an odor like that of the essential oil present in them. They are smaller than those of the true star anise. The plant flowers in April. At a distance the flower

[6] *Flora Japonica,* 1835, p. 5.

[7] *Het Gezag van Kaempfer, Thunberg, Linnaaeus en anderen, Omtrent den bot. oorsprong van der Ster-anijs des Handels;* Tschirch, *Handb. d. Pharmakog.* II, 2 (1913), p. 1215.

[8] *Bot. Magazine,* 1888; Tschirch, *Handb. d. Pharmakog.* II, 2, p. 1215.

[1] *Pharm. Jour.* 40 (1880-1881), pp. 489-91.

[2] *Pharm. Jour.* 40 (1880-1881), pp. 1066.

[3] *Des Illicium en Genera, de la badiane et de son huile essentielle en particulier,* Montpellier. A thesis (1886).

[4] *Chiugai iji shipo,* Tokyo (*Medical news of the world*), (1890), pp. 1245-48; also pp. 1317-20.

looks like that of the narcissus. It is about an inch and a half in diameter. The petals are greenish, or very slightly yellowish-white and have a wax-like appearance; they are from 1-3 cm. long and 5 cm. broad, 12 to 20 in number with 15 to 20 stamens.

Chinese Synonyms:	**Mang Tsao**	莽艸	**(mad herb)**
	Shu Mang	鼠莽	**(rat poison)**
	Ao Woo Soo	媼烏蘇	
	Chun Tsao	春艸	**(Spring herb)**
Japanese Synonyms:	**Shikimi**	毒シキミ	**Sikimi** 梻
	Ashikimi	惡實	**(evil fruit)**
	Seke	石桂	
	Kake	紅圭	
	Yoka	葉花	
	Koyo	香葉	
	Tse	栂	
	Tse Zden so	佛前艸	**(herb before the temple)**
	Yin Ba	因播	
	Hari ma	播磨	
	Tsi ku sen	筑前	
	Yeun kiang	遠江	

Hackijo 豆州八丈島

The fruit is about one-third less in diameter than that of *Illicium verum* [5]—the diameter is about 25 mm. while that of *Illicium verum* is about 32 mm.[6] It consists of 8 carpels arranged side by side in a close circle which has a depth of about 0.5 cm. Each carpel has on the upper side the pistil. In the unripe condition the fruit is green, juicy, and contains much essential oil. When it commences to ripen in the autumn, the carpel rapidly dries up especially on the dorsal side, shrivels, and becomes of a red-brown color, and opens so rapidly along the upper side that the seeds are very often hurled out with considerable force. Generally only a few of the carpels develop to maturity and the fruit is, therefore, very irregular. However, according to Menir [7] and Oberdörffer [8] they are quite regularly developed and rarely abortive. According to the writer's experience the partially developed carpels occur much more commonly among the Japanese than the Chinese star anise, yet it was much easier to find some completely developed fruits of the former than the latter. In other words the fruits of *Illicium verum* are more uniformly matured than those of *Illicium religiosum*. The fruit has a less agreeable odor than the bark and a taste somewhat saline and decidedly bitter, faintly resembling cardamom.

Habitat of the plant. *Illicium religiosum* is indigenous in Szechaung, China and was introduced in ancient times into Japan by Buddhist priests (Kaempfer). Now it grows wild in Japan on the mountain sides near Nagasaki, Yokosuka, and Tokyo and in large numbers upon the Island of Hackijo. In earlier times it was found also in the provinces of Izu, Sayami, Enshu, Tamba, Mussashi, Hizen, Chozhu, etc. The plant is frequently cultivated in the gardens of eastern France.[9]

Uses. In China the poisonous star anise is used as local application in the treatment of toothache; also in certain forms of dermatitis, parasitism, etc. As a fish poison the powder of the leaves is thrown into the water and, when intoxicated, the fishes are easily caught. When cooked these fishes are said not to be poisonous to the people who eat them. It was also used to destroy rats. As already

[5] Vogl, *Mittheil. des Wien. Med. Dokt. Coll.* 7 (1881), p. 167.

[6] Tschirch und Oesterle, *Anatom. Atlas d. Pharmakog. u. Nahrungsm.* (1900), pp. 241-44.

[7] *Jour. de Med. de l'Ouest. Nantes.* 8 (1884), 2 S., p. 113.

[8] *Pharm. Centralb.* 22 (1881), pp. 162, 177, 276 and 400.

[9] Murakoshi, *Flora of Japan* (1925), p. 592.

stated the Japanese plant the tree around temples, the flowers being used for the adornment of the altar. They are also displayed in consecrated vessels for the use in religious feasts. The tree is also planted near graves, because of the general veneration for the tree, perhaps also on the ground that as a poisonous plant it has the reputed power to keep away insects and wild animals. The aromatic bark is used by the Buddhists as an ingredient in pastilles which are so made as to burn a certain length of time and thus serve as a sort of chronometer. The fruit is not used as a spice nor for any other purposes, but the oil expressed from the seed is used as a cheap lighting material and as a lubricating oil.[10]

Morphology

The fruit of *Illicium religiosum* was only briefly described by Kaempfer,[1] Baillon,[2] Siebold,[3] Loureire,[4] and Berg.[5] After the occurrence of the poisoning cases at Leeuwarden in the Netherlands in 1880, the morphology of this fruit was fully investigated: by Holmes,[6] Husemann,[7] and Geerts,[8] in 1880; Vogl,[9 10 11] Eykman,[12] and Oberdoerffer,[13] in 1881; Pabst,[14] in 1883; Ménier,[15] in 1884; Tambon,[16] in 1886; Flückiger,[17] in 1891; Waage, [18] in 1893; Collin

[10] Husemann, *Pharm. Jour.* 40 (1880-81), pp. 453-54.

[1] *Loc. cit.*

[2] *Le Regne végétale,* (1864-1869), *Flora médicale,* vol. 5, p. 143; and vol. 6, p. 20.

[3] Siebold, *Flora Japonica* (1871), p. 5.

[4] *Flora Cochinchinensis* 1, p. 353 (1790).

[5] *Pharmakog. d. Pflan. u. Thiere,* 5th ed. (1879), p. 361.

[6] *Pharm. Jour.* 40 (1880-1881), p. 489.

[7] *Ibid.,* p. 453.

[8] *N. Tijdsch. v. Pharm.* 1880, p. 298; *Pharm. Weekbl.* 17 no. 15; *Jahresb. d. Pharmakogn.,* 1880, p. 50.

[9] *Mitth. d. Wien. Med. Dokt. Coll.* 7 (1881), p. 167-173.

[10] *Commentar z. 7 Ausg. d. Oesterreich. Pharmacopoee* II, (1892), p. 137.

[11] *Nahrungs- u. Genussm. mit besonderer Berueck. d. mikroscop. Untersuchung* (1899), pp. 465-76.

[12] *Pharm. Jour.* 40 (1880-1881), p. 1066.

[13] *Pharm. Zeitschr.* 22 (1881), pp. 162, 177, 276, and 400.

[14] *Koeler's Medizinal Pflanzen,* I (1883), p. 117.

[15] *Jour. de Med. de l'Ouest. Nantes* (1884), 2d s. 8, p. 113.

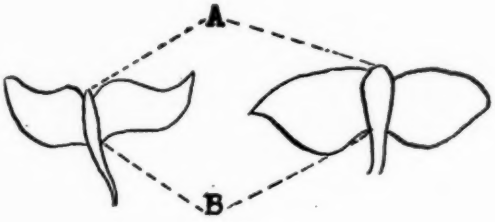
[16] *Des Illicium en général, de la badiane et de son huile essen. en particulier.* Thèse, Montpellier (1886).

[17] *Pharmkogn. d. Pflanz.* (1891), 3d ed. pp. 932-37.

[18] *Ber. d. Pharm. Gesells.* 3 (1893), p. 161.

and Planchon [19] and Lauren [20] in 1896; Lenz,[21] in 1899; Tschirch and Oesterle,[22] and Villiers and Collin,[23] in 1900; Beuttner [24] and Hartwich,[25] in 1907. Illustrations are found in the articles by Kaempfer, Holmes, Vogl, Tambon, Collin and Planchon, and Villiers and Collin. The most detailed illustrations by Vogl are reproduced in Winton's Microscopy of Foods and Drugs.[26] In order to make the description and comparison of the fruits more readily comprehensible samples of both *Illicium religiosum* and *Illicium verum* were selected from sixty pound lots and photographed.

The whole fruit. On the average the fruit of the poisonous star anise is smaller than that of the genuine, the diameter of the former being from 16-33 mm., mostly about 25 mm., according to Vogl and from 15 to 31 mm., mostly from 22 to 29 mm., according to Hartwich, the diameter of the latter being from 22 mm. to 42 mm., mostly about 30 mm., according to Vogl and from 17 to 40 mm., mostly from 30 to 37 mm., according to Hartwich. Vogl's values are quoted by Tschirch and Oesterle. The color of the poisonous fruit is lighter and the structure is less woody than that of the genuine. As a rule only a few of the carpels are developed to maturity. Abortive car-



Illicium religiosum **Illicium Verum**

[19] *Les Drogues simples d'origine végétale,* (1896), 2, pp. 890-93.
[20] *Scheiz. Wochenschr. f. Chem. u. Pharm.* 34 (1896), pp. 278-81; 37 (1899), pp. 45-50.
[21] *Ibid.*
[22] *Anatom. Atlas,* (1900), pp. 241-44.
[23] *Traité des alterations et falsif. des subs. aliment.* 1900, pp. 295-303.
[24] *Schweiz. Wochenschr.* 45 (1907), pp. 277-82.
[25] *Ibid.,* 45 (1907), pp. 798-809, 39 (1901), p. 104.
[26] *Microscopy of vegetable Foods,* 2d ed. (1916), pp. 572-73.

pels are rare. The middle of the lower side, A, either projects or is at the same level as the base of the carpel as shown in the figure which was taken from Tschirch's *Handbuch der Pharmakognosie,* II, 2, p. 1216. The fruit is about 0.5 cm. high.

The carpel. The carpel is from 10 to 13 mm. long and 5 to 8 mm. wide forming a sharp and thin point curved upward. It is more woody and rougher on the surface, more wrinkled and shriveled, lighter in color and more boat-like and compressed than the rosette-formed star anise. When dried it opens at the dehiscent line more than the true star anise so that the lighter-colored interior is more exposed. The color of the carpel is a shining red-brown. The carpels are usually shrunk upon one another. Its taste is bitter, somewhat saline, faintly resembling that of cardamom, but disagreeable. The odor is spicy but not at all like anise.

The columella. The upper side of the columella, B, is a sharp point and usually does not reach the same height as the carpels but sinks to a depth as shown in the above illustration (Lenz).

The fruit stem. The stem is generally straight (Moeller)[27] and lacking (Oberdoerffer). It is 10-13 mm. long, 1 mm. thick, with a light, circular cork nobe at both ends while the middle part is of uniform size. It is grayish-brown or reddish-brown deeply striated with longitudinal furrows (Vogl).

The seed. The size and the shape of the seed varies with the degree of ripeness. Usually it is about 0.7 cm. long and 0.5 cm. broad. It is provided with a hard testa and occurs one in a carpel. It is bulgy round, full, less compressed, with a brown color, but lighter than that of a true star anise. The wart-like hilum is light yellow nearly white (Vogl). The apex of the seed is not rounded, but at the end of the keel terminates in a raised point, which is not the case in true star anise. The exception to this becomes more frequent in the larger well-developed seeds (Eykman). It tastes oily and has no aromatic odor.

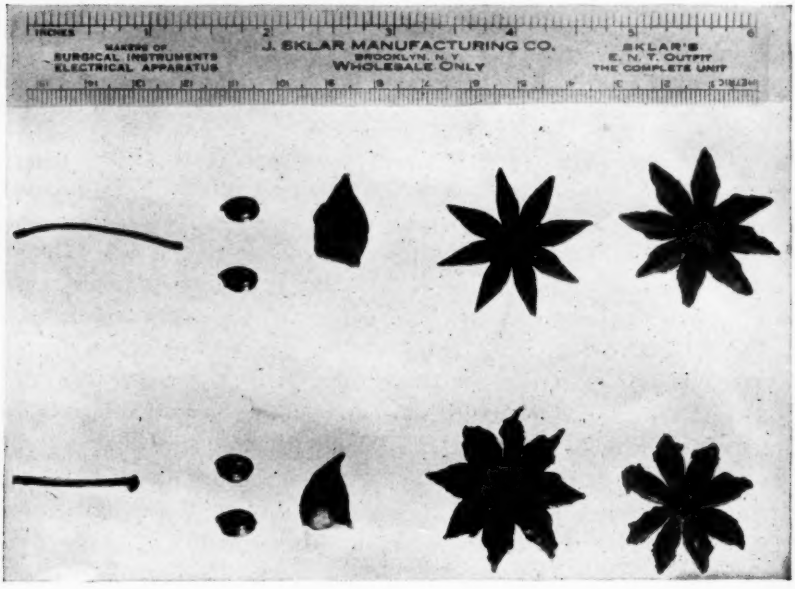
Histology*

Although in even a superficial comparison of a sample of shikimi fruit with one of true star anise differences of form can not be de-

[27] *Mikroskopie d. Nahrungs- u. Genussm.* (1886), p. 276.

* Acknowledgment is hereby made to Dr. R. H. Denniston under whose directions this study was performed. He also made all the slides.

nied, yet none of the morphological features, which are very probably connected with the age, the manner and time of collection, the conveyance, the climate, etc. (Eykman), can be regarded as sufficiently constant to tell apart with certainty the two drugs in a mixture. For this reason many authors have thought a histological investigation desirable. Such examinations have been made by Tambon,[1] in 1886; Flückiger,[2] in 1891; Pfister,[3] in 1892; Waage,[4] in 1893; Lauren,[5] also Collin and Planchon,[6] in 1896; Lenz[7] also Vogl,[8] in 1899;



[1] *Des Illicium en général, de la badiane et de son huile en particulier.* Thèse, Montpellier, 1886.

[2] *Pharmakognosie des Pflanzenr.* 3d ed. (1891), pp. 932-37.

[3] *Vierteljahreschr. Naturforsch. Gesell.*, Zürich, 37 (1892), pp. 313-322; *Schweiz. Wochenschr.* 32 (1894), p. 233.

[4] *Ber. d. Pharm. Gesell.* 3 (1893), p. 161.

[5] *Les Drogues simples d'origine végétale*, 1896, 2, p. 890.

[6] *Schweiz. Wochenschr.* 34 (1896), p. 278.

[7] *Ibid.*, 37 (1899), pp. 45-50; Pharm. Ztg. 44, pp. 44-46.

[8] *Mittheil. des Med. Coll.* 7 (1881), pp. 167-73; *Nahrungs- u. Genussm.* 1899, pp. 465-76.

Tschirch and Oesterle,[9] in 1900; Hartwich, [10] in 1907 and Plahls,[11] in 1911.

According to Tschirch and Oesterle there is no difference in the anatomical structure of the fruit of *Illicium verum* and that of *Illicium religiosum*. For this reason the microscopic picture of the former only is given in their Anatomical Atlas. Although others, like Tambon, Collin and Planchon, and Vogl, have published drawings of the structure of the latter, they are by no means complete. In order to make comparison easier sections of the carpel, seed and stem of *Illicium religiosum* were made and drawn.

Palisade cells of the endocarp are mostly from 348-360 μ (Plahls), 325-400 μ. (Tschirch and Oesterle) and occasionsally 180-260 μ (Hartwich) long and are highest on the under side of the fruit cavity (the side furthest from the dehiscent surface) passing abruptly into the cells of the dehiscence surface. In the stem and fruit column there are rounded stone cells (longest up to 300 μ mostly from 103 to 164 μ Lenz) with uniformly thickened wall; while in the star anise the palisade cells of the endocarp are longest (up to 600 μ) near the dehiscence surface and gradually pass into the cells of that surface.

Astrocleides are present only in the fruit column of the true but not in that of the false star anise (Collin and Planchon). According to Pfister the most striking anatomical difference between the seeds of the two species is to be found in the aleurone grains. Those in the *Illicium religiosum* are smooth, lustrous and contain one to three distinct big crystalloids (15-20 μ for the larger and 4-8 μ for the smallest) and many globoids. While in *Illicium verum* they are rougher on the surface and contain generally globoids rarely single crystalloids. Tschirch and Oesterle make the same statement. But these statements are not proved by Waage. The writer had the same difficulty as Waage, that is, no distinct difference could be seen. The reason is probably that the aleurone grains are so minute that even under the best microscope available in the laboratory they are not readily seen.

To the writer, the features which will render the differentiation between the two fruits easily are the oil cells and the cross section of the fruit stems. The former are present abundantly in the true

[9] *Anatom. Atlas*, 1900, pp. 241-44.

[10] *Sweiz. Wochenschr.* 45 (1907), pp. 798-812.

[11] *Arch. f. Chem u. Mikrosk.* (1911), cited by Tschirch in his *Handb. d. Pharmakog.* II, 2, p. 1217.

star anise, but few in number in the other. The cross section of the stem of shikimi fruit is very irregular while that of the true star anise is of uniformly circular shape.

This study was discontinued before commencement 1927. In the issue for September 13, 1928, the following article appeared in the *Pharmazeutische Zentrhalle:* Zur Mikrochemie von Illicium verum Hook, und Illicium religiosum Sieb. By Editha Siersch. The paper is a contribution from the Institute for Plant Physiology of the University of Vienna.

Material. Several attempts to secure poisonous star anise from China resulted in the delivery of the true star anise. The materials thus obtained were used for a comparative study of the two drugs. Finally, through the personal efforts of Mr. S. S. Chi, 14 ko. of the desired material were obtained in Peking. It was identified as *Illicium religiosum* by Dr. B. E. Read, the well known investigator of Chinese drugs in the Peking Union Medical College. The carpels were irregular, the taste bitter and odor spicy, whereas true star anise has more regular carpels, a pleasant odor and a sweet taste. Certainty as to its poisonous character was obtained by a pharmacological test. 5 g. of powdered drug were macerated with 75 cc. of alcohol for 24 hours. 25 cc. of the solution thus obtained were evaporated under greatly reduced pressure to about 1 cc. and the residue diluted with water to about 3 cc. one-half of this solution, representing 0.83 g. of drug, was injected subcutaneously into a rat weighing about 200 grams. Five minutes after injection the animal showed symptoms of distress. It died within two hours. Another rat which was given an injection similarly prepared from 4 g. of true star anise was still living after two weeks.

Proportion of seed to carpel. A. Fifty and one hundred gram samples respectively were weighed off without selection and separated into seed and carpel, each part weighed and the percentage as to the whole computed.

	Wt. of sample	*Wt. of seed*	*Percentage of seed*	*Wt. of carpel*	*Percentage of carpel*
1.	50 g.	3.8 g.	7.6 p.c.	45.5 g.	92.4 p.c.
2.	100 "	7.0 "	7.0 "	93.0 "	93.0 "
3.	100 "	7.5 "	7.4 "	91.8 "	92.5 "
	Average		7.4 "		92.6 "

B. Twelve complete and well developed fruits were selected and each weighed separately. Each fruit was then separated into carpels and seeds and the carpels and seeds of each fruit weighed separately.

No.	*Wt. of fruit*	*Wt. of 8 seeds*	*Percentage of seed*	*Av. wt. of a single seed*
1.	1.5468 g.	0.5689 g.	36.90 p.c.	0.0712 g.
2.	1.5329 "	0.5216 "	34.02 "	0.0652 "
3.	1.5658 "	0.5028 "	32.17 "	0.0629 "
4.	1.8004 "	0.5674 "	31.52 "	0.0709 "
5.	1.4584 "	0.4589 "	31.43 "	0.0574 "
6.	2.1199 "	0.6544 "	30.87 "	0.0818 "
7.	2.2094 "	0.6134 "	27.77 "	0.0767 "
8.	2.1071 "	0.5834 "	27.73 "	0.0729 "
9.	2.1901 "	0.6744 "	30.79 "	0.0843 "
10.	1.5200 "	0.6026 "	39.64 "	0.0753 "
11.	1.6564 "	0.5859 "	35.38 "	0.0782 "
12.	1.5959 "	0.5684 "	35.61 "	0.0711 "
Average	1.7755 g.	0.5749 g.	32.82 p.c.	0.0719 g.

The heaviest fruit (No. 7) weighed 2.2094 g. or 0.4339 g. *i. e.* 24.43 p.c. more than the average.

The lightest fruit (No. 5) weighed 1.4584 g. or 0.7510 g. *i. e.* 42.29 p.c. less than the average.

It becomes apparent from the average weights of true and poisonous star anise fruits, *viz.* 1.5929 g. and 1.7755 g. respectively that the average difference of 0.1826 g. is appreciably less than the fluctuations between the weights of fruits of the same species.

Moisture determination. The water content of the air dried drug was determined by means of the xylene method[1] using 10 g. of powdered material in each case.

Two determinations for the carpel yielded 3.5 p.c. and 4.0 p.c. respectively.

Two determinations for the seed yielded 4.8 and 5.2 p.c. respectively.

[1] A. L. Dean, *Forest Service Circular* 134 (1908), U. S. Dept. of Agriculture.

K. K. Chen [2] found 3.44 p.c. for the seed and 3.46 p.c. for the carpel.

Ash determination. The determinations were made separately for carpel and seed.

3.5039 g. of carpel yielded 0.0027 g. (=0.077 p.c.) of ash insoluble in acid and 0.1020 g. (=3.367 p.c.) of total ash.

3.8742 g. of carpel yielded 0.0016 g. (=0.042 p.c.) of ash insoluble in acid and 0.1290 g. (=3.356 p.c.) of total ash.

3.8378 g. of seed yielded 0.0026 g. (=0.068 p.c.) of ash insoluble in acid and 0.0554 g. (=1.445 p.c.) of total ash.

4.0875 g. of seed yielded 0.0040 g. (=0.098 p.c.) of ash insoluble in acid and 0.0600 g. (=1.443 p.c.) of total ash.

The difference in total ash content of carpel and seed is very marked, that of the acid insoluble ash is not so great.

K. K. Chen [1] found 0.1921 p.c. acid-insoluble ash and 1.472 p.c. total ash in the seed; also 0.172 p.c. of acid-insoluble ash and 3.432 p.c. total ash in the carpel.

Extraction of seeds and carpels with selective solvents. Two samples each of 15 grams of seed and 20 grams of carpel, both in fine powder, were extracted successively with petroleum ether, ether, alcohol, and water. With the exception of the aqueous extract, the extracts were allowed to evaporate spontaneously and dried over sulphuric acid. In the case of the aqueous extract, gentle heat was used to evaporate the solvent. The results are herewith recorded:

A. Seed

Solvent	*Wt. of extract*		*Percentage of extract*		*Average percentage*
	I	II	I	II	
Petr. ether	3.1622 g.	2.9234 g.	21.12	19.49	20.31
Ether	0.2989 "	0.2744 "	11.99	1.83	1.91
Alcohol	0.6185 "	0.6295 "	4.1	4.19	4.16
Water	0.2230 "	0.2351 "	1.49	1.56	1.52
Total extractives					27.90 pc.

[2] *Jour. A. Ph. A.* 15 (1926), p. 625.

[1] *Jour. A. Ph. A.* 15 (1926), p. 625.

B. Carpel

Solvent	*Wt. of extract*		*Percentage of extract*		*Average percentage*
	I	II	I	II	
Petr. ether	0.2876 g.	0.2910 g.	1.44	1.46	1.45
Ether	2.8620 "	3.2370 "	14.31	16.18	15.25
Alcohol	4.5635 "	4.2750 "	22.82	21.38	22.10
Water	1.2280 "	1.5135 "	6.14	7.57	6.76
Total extractives					44.56 p.c

The petroleum ether extract of the seed consists of a yellow oil without the characteristic odor of the fruit. It thickens on standing. The ethereal extract is a yellowish-brown powder. The alcoholic extract is dark reddish-brown resembling a resin.

The petroleum ether extract of the carpel is a greenish-yellow oil which on standing in a desiccator over sulphuric acid becomes semi-solid. The ethereal extract consists of a white crystalline material, probably shikimic acid, which is only sparingly soluble in cold ether, but to a greater extent in the hot solvent. This may also account for the fact that the ethereal extraction took more than 100 hours before exhaustion was reached. The alcoholic extract consists of a resinous residue which is thick and sticky and of a reddish-brown color.

The aqueous extracts of both seed and carpel are brownish-red, solid, and very readily pulverized.

Extraction with alcohol. 14.5 ko. of finely powdered fruit were exhausted with alcohol in a Lloyd extractor. After the removal of the residual alcohol from the extract drawn from the apparatus, the extract was shaken repeatedly with heptane and the liquid portion separated by straining. The filtrate separated into two layers: a hydrocarbon layer and an aqueous layer.

From the former the hydrocarbon was recovered by distillation. Steam was passed through the residue thus separating it into a volatile oil (A) and a residual fatty oil (B). Of the former 37 g. (=0.25 p.c. of the original drug) were obtained and of the latter 240 g. (=1.65 p.c.).

The aqueous filtrate was shaken successively with ether and chloroform. The solid material in the strainer was also washed with ether and chloroform. The ether washings of both aqueous filtrate and solid residue were mixed, the chloroform washings likewise. The solvents were recovered. Thus four different substances were obtained.

C. Material soluble in ether
D. Material soluble in chloroform
E. Aqueous liquid shaken with both ether and chloroform
F. Solid material washed with both ether and chloroform.

A. *Volatile oil.* As previously stated, 37 g. of volatile oil were obtained by steam distillation from the oily material separated from the alcoholic extract by shaking and washing with heptane and removal of the hydrocarbon. d21° =0.9834; n_D25° =1.4874; a_D =5.2° at 21° in a 100 mm. tube; it did not congeal in a freezing mixture at −10°, A. V. =0.42; S. V. =28.83.

The volatile oil was prepared by Eykman,[1] in 1881, by Schimmel & Co.,[2] in 1893 and 1909, by Tardy,[3] in 1902 and K. K. Chen,[4] in 1926. For better comparison the results are herewith tabulated together with those of the investigators recorded:

	Eykman	*S. & Co.*	*Tardy*	*K. K. Chen*	*S. Y. Chen*
Yield		1.00 p.c.	0.4 p.c.	0.6 p.c.	0.25 p.c.
d	1.006	0.984–0.994		0.9905* 0.9790†	0.9834
n_D				1.5007* 1.4960†	11.4874
a_D	−8.6°	−0.50°		−6.159°* −6.539°†	−5.20°
Cong. pt.	not at −20°	−18°		not at −6°	not at −10°
A. V.		1.8		4.25* 4.28†	0.42
S. V.		12.9		37.99* 24.69†	28.83

[1] *Pharm. Jour.* 41 (1881), p. 1048.
[2] *Bericht S. & Co.*, Oct., 1893, p. 46; Apr., 1909, p. 51.
[3] *Étude analytique sur quelques essences des génere anisique.* Thèse, Paris, 1902.
[4] *Jour. A. Ph. A.* 15 (1926), p. 865.
* Original oil.
† Cohobated oil.

B. *Fatty oil.* The fatty oil remaining after the distillation of the volatile from the heptane extract of the alcoholic extract of the entire fruit was thick and green. Its density at 21° was 0.9268; A. V. = 17.25 and 17.79 respectively in two determinations; S. V. = 210.2 and 210.9 respectively, hence E. V. = 210.6–17.54 or 193.1; I. V. = 101.0 and 103.9 respectively.

The fatty oil has been prepared by Bulir [1] (1912) and Chen [2] (1926).

Saponification of the fatty oil. 220 grams of the fatty oil were heated with an excess of alcoholic potash on a water bath for one hour. At the end of this period the alcohol was distilled off. The residue which formed a semi-solid cake after cooling was dissolved in water with the aid of heat. Having been allowed to resume room temperature once more the aqueous solution was shaken several times with ether. Upon spontaneous evaporation of the solvent, a yellow semi-solid substance with an aromatic odor resembling that of ginger, was obtained. (Unsaponifiable matter.)

After being washed with ether, the aqueous alkaline solution containing the potassium soap was neutralized with 1:1 HCl and the free organic acid thus liberated was separated from the aqueous solution mechanically.

Separation of solid and liquid fatty acids by means of lead-salt-petroleum-ether method. (Gusserow [3]-Varrentrapp [4] method.) The free acid was neutralized with aqueous potassa using phenolphthalein as indicator. 140 g. of lead acetate, dissolved in 700 cc. of water at boiling temperature, were added gradually to the well-stirred neutral salt of the fatty acids. The stirring was continued until the solution was cold when a solid cake had formed. After having been washed several times with warm water the lead soap or plaster was separated from the water, first by draining and finally by heating on a water bath under reduced pressure. To the lead soap petroleum ether was added. This solvent was chosen instead of ether because of its less solvent action than ether upon the lead salts of some of the solid acids as suggested by Twitchell [5] & Lane.[6] The extraction of

[1] *Zeitsch. f. Unters. d. Nahrungs- u. Genussm.* 24, p. 309; through *Analyst* 37 (1912) p. 495.

[2] *Loc. cit.*

[3] *Ann.* 27 (1838), p. 153.

[4] *Ibidem*, 35 (1840), p. 197.

[5] *Jour. A. C. S.* 17 (1895), p. 209; also *Jour. S. C. I.* 14 (1895), p. 515.

[6] *J. S. C. I.* 26 (1907), p. 597.

the soluble lead soap of the unsaturated acids by the petroleum ether was accomplished by heating the mixture to boiling under a reflux-condenser for half an hour and placing the flask in an ice box over night. The undissolved portion was separated by filtration.

Solid fatty acids. The lead soap which was insoluble in petroleum ether was decomposed under ether with 1:1 HCl and the ether solution containing the acids was washed with water until the solution was neutral to litmus paper.

After the removal of the ether a solid green cake amounting to 40.0 g. was left. The acid value was determined. Due to the slight solubility of this acid in cold alcohol a mixture of alcohol and ether (1:1) was used as solvent in the acid value determination. The results are herewith tabulated:

Sample	(1)	0.3271 g. A. V.	184.9
	(2)	0.1806 g. A. V.	184.1
		Average	184.5
Calculated acid value for stearic acid =			196.1
		for palmitic acid =	217.5

This low A. V. indicates the presence of some acid with higher molecular weight than stearic acid.

Separation of solid fatty acids. The solid cake of acids was crystallized from a 20 p.c. solution in absolute alcohol. The greenish acid which thus separated amounted to 0.4 g. It had a m.p. of 73–76°. After repeated recrystallization the m.p. rose to 82°; the following acid values were found:

Sample	(1)	0.0728 g. A. V.	117.2
	(2)	0.1172 g. A. V.	117.9
		Average	117.6

An attempt was made to remove completely the greenish color of this acid by filtering through charcoal but was not very satisfactory. The alcoholic filtrate was then evaporated and the residue was recrystallized from ethyl acetate; this solvent being used by F. B. Power in his isolation of behenic acid from *Micromeria Chamissonis.* The acid thus recrystallized has a m.p. of 82.5° and an acid value (Sample 0.4502 g.) of 118.4.

Although it is still colored green, the slight increase of m.p. and in A. V. after filtration through charcoal and recrystallization from

ethyl acetate indicate it to be purer than before. Its molecular weight was computed at 473.7. The following data are taken from Lewkowitsch, *Tech. & anal. of fats, oils and waxes.*[7]

M. W. for	$C_{32}H_{64}O_2$ is 480.0		
M. W. for melissic acid	$C_{30}H_{60}O_2$ is 452	m.p.	91–98°
M. W. for psyllostearylic acid	$C_{31}H_{64}O_2$ is 466 / $C_{33}H_{66}O_2$ is 494	m.p.	94–95°
M. W. for geomyricin	$C_{34}H_{68}O_2$ is 508	m.p.	80–83°

Stearic and palmitic acids. The filtrate from the acid was evaporated to half its volume and placed in an ice box over night. A crop of crystals was formed. On recrystallization from alcohol an almost colorless acid was obtained. It melted at 56° and has the following acid value:

Sample (1)	0.0659 g.	A. V.	201.6
(2)	0.0615 g.	A. V.	202.0
	Average		201.8

The last filtrate was decolorized by means of charcoal and crystallized by cooling. An acid melting at 56° was obtained. Its acid value is 203.8. Since this acid has the same m.p. and approximately an equal A. V. with the previous one they were mixed.

While trying to separate the constituents of this acid mixture, namely the palmitic acid and stearic acids, a part of this mixture was dissolved in 50 p.c. warm alcohol following the suggestion of Lewkowitsch. On cooling at room temperature most of the fatty acid was separated and filtered. The filtrate gave another crop of crystals (only 0.15 g. from 10 g. of mixture) on cooling in an ice mixture. The following constants for both acids were determined:

Acid insol. in 50 p.c. alcohol m.p. 57° A. V. 202.3
Acid sol. in 50 p.c. alcohol m.p. 57° A. V. 208.5

These results show that neither of the two components is pure palmitic or stearic acid.

Taking 201.8 as the A. V. the percentage of palmitic and stearic acid in the total mixture of 40.0 grams can be calculated.

Total acid	40.0 g.	
Purified acid	0.5 g. =	1.2 p.c.
Stearic acid		80.0 p.c.
Palmitic acid		19.8 p.c.

[7] *Tech. & anal. of fats, oils and waxes,* 6th ed. (1923), p. 118.

According to Lewkowitsch the melting points of mixtures of palmitic and stearic acids are as tabulated:

Stearic	*Palmitic*	*m.p.*
80 p.c.	20 p.c.	64.51°
55 p.c.	45 p.c.	57.0°

Separation of the liquid acids. The petroleum ether solution obtained by filtering off the insoluble lead soap of the saturated acid was treated with HCl (1:1) and the precipitate thrown down filtered off. The acid solution was washed several times with water until all the mineral acid had been removed. The solution was next dried over anhydrous sodium sulphate, the solvent distilled off, and the residue dissolved in ether. 50 cc. of 735 cc. of this ether solution, upon evaporation to constant weight, left 5.4414 g. as oily residue. The total liquid acid therefore, amounts to 76.2 grams. The following constants were determined:

Acid value	134.4
Iodine value [8]	97.95
I. V. of oleic acid is	90.07

This iodine value shows the presence of some acid which is less saturated than oleic.

Bromination of the liquid acid. Farnsteiner's method was used.[9] To the ether solution of the acid 40 cc. of glacial acetic acid were added and the mixture was cooled to −10°. Bromine was dropped in with constant shaking. When the solution had acquired a permanent color of bromine it was cooled in an ice box over night. 20 cc. of bromine were used. A small amount of white precipitate had deposited and was identified as a lead compound.

Tetrabromide. After the removal of the precipitate the ether solution was washed with saturated solution of $Na_2S_2O_3$ until the excess of free bromine was completely removed. The trace of $Na_2S_2O_3$ was in turn removed by washing with pure water and finally the moisture by means of anhydrous $Na_2S\,O_4$. The ether was distilled off and the residue treated with hot petroleum ether. After standing for 3 hours 40 grams were obtained as a precipitate. This precipitate was purified by dissolving in benzene, filtering through

[8] The U. S. P. method was used.

[9] *Zeitsch. f. Unters. d. Nahrungsm. u. Genussm.* 2 (1899), p. 1.

charcoal, and recrystallizing from the same solvent. A perfectly white compound was thus obtained which had a m.p. of 113.5°. The tetrabromide of linoleic acid melts at 114°.

The bromine content was determined according to Stepanow.[10]

Sample	(1)	0.2274 g.	Br.	53.09 p.c.
	(2)	0.2302 g.	Br.	52.77 p.c.
		Average		52.93 p.c.

Tetrabrom linoleic acid contains 53.33 p.c. Br.

Dibrom compound. The solution after the removal of the tetrabromide was placed in an ice box for two days but no more precipitate was obtained. It was then evaporated spontaneously and finally on a steam bath to remove the last traces of petroleum ether. In this highly colored liquid the bromine content was determined.

Sample	(1)	0.3321 g.	Br. =	36.95 p.c.
	(2)	0.3074 g.	Br. =	38.38 p.c.
	(3)	0.3044 g.	Br. =	36.95 p.c.
Br. in dibrom oleic acid =				36.36 p.c.

Non-saponifiable matter. Upon evaporation of the ethereal solution 9 grams were obtained as a yellowish soft material with a ginger-like odor. Charcoal did not remove any appreciable amount of color. Hot alcohol yielded a small amount of soft crystals melting at 70–73° and an oily residue (7 g.).

The crystals gave the Salkowski-Liebermann[11] reaction for phytosterol. Attempts to recrystallize it from alcohol resulted, for the most part, in jelly-like masses. Treatment with petroleum ether, however, made possible a separation into a soluble portion (70 mg.) that melted at 63–64°, and an insoluble portion (40 mg.) that melted at 78–81°.

From the fat of rice bran, Nabenhauer and Anderson[12] have recently isolated myricyl alcohol which melted at 80° in the impure condition and at 85° after several recrystallizations. Possibly the portion insoluble in petroleum ether melting at 78–81° is identical with this alcohol. The acetate prepared, if it was such, melted at 64°, whereas myricyl acetate is said to melt at 73°. However, the amount available was too small to admit of purification.

[10] *Ber.* 39 (1906), p. 4056.
[11] *Zeitsch. f. physiol. Chem.* 57 (1908), p. 515.
[12] *Jour. A. C. S.* 48 (1926), p. 2972.

From the unsaponifiable matter of the fat of rice bran Weinhage[13] isolated a hydrocarbon $C_{27}H_{48}$ which melted at 79.5° to 80.5°.

The combined mother liquids from recrystallization were reduced to an alcoholic strength of about 70 p.c. when practically all of the material separated. It had a m.p. of 121–126°. After recrystallization from alcohol the m.p. was raised to 134–135°. Sitosterol melts at 135°.[14] An acetate prepared from the laminar crystals which, under the microscope appeared typically sitosterol-like, melted at 100°, whereas sitosterol acetate melts at 125°. Again the amount was too small to admit of purification.

Glycerin. After the organic acids had been removed from the potassium soap, the aqueous portion was neutralized with sodium hydroxide and evaporated on a water bath. When the solution was fairly concentrated the salt which had separated out was filtered off, the coloring matter taken up by means of charcoal and the clear solution was distilled under a pressure of 60 mm. When the temperature reached 148° nothing more distilled over and the residue was taken up with ether. On the removal of the solvent the ethereal solution yielded a thick liquid with a sweet taste. Upon this liquid the following tests were made:

When about 1 g. of the liquid was heated in a test tube with 2 g. of $KHSO_4$ vapors having the odor of acrolein were evolved. These vapors reduced ammoniacal silver solution very readily and reddened Schiff's reagent.

Following the method devised by Chapman for the identification of glycerol in tobacco, about one-half gram of this liquid was gently heated with α-napthol isocynate in a dry tube until a vigorous reaction took place. This solid mass was treated with hot pyridine and the insoluble material was filtered off. On cooling the pyridine solution yielded a white crystalline powder melting at 260°.

A similar compound made from commercial glycerin melted at 268°. According to Chapman the glycerol urethane melts at 278–280° although softening may commence at about 270° or even below.

Bickel and French made the same urethane from glycerol and isocynate, but instead of pyridine they used ligroin boiling at 100–120°. The melting point of the urethane was found at 191–192°.

[13] *Zeitsch. f. physiol. Chem.* 100 (1917), p. 159.
[14] *Windaus and Hauth, Ber.* 39 (1906), p. 4379.

Since dinaphthyl urea is easily formed in the presence of moisture the compound obtained by Chapman might be dinaphthyl urea which melts at 268°.

To repeat Bickel and French's experiment some urethane was made from commercial glycerin and treated with boiling heptane since no ligroin boiling at 100–120° was readily available. Nothing separated from the heptane solution on cooling, and the solvent was removed by evaporation at 60°. The residue had no definite melting point.

Tests for toxicity upon rats. In order to ascertain in which of the different portions, into which the alcoholic extract of the drug had been separated, the toxic principle is located pharmacological tests were made upon white rats.

1. *Heptane soluble portion.* After the removal of the solvent from the heptane soluble portion 0.225 gram of the residue which constituted a green oil, were shaken vigorously with 4.5 cc. of water. 2 cc. representing 0.10 g. of the original extract were injected subcutaneously into a white rat of 280 g. Twenty minutes after injection the animal showed distress: paralysis of the hind legs and violent convulsions in the opisthotonus position. It died 15 minutes after the appearance of the first symptom.

2. *Ether soluble portion.* 1.0 cc. of the aqueous solution prepared from 0.1 gram of the dried ethereal extract was injected subcutaneously into a white rat of 260 g. Twenty-four minutes after injection the animal sat down showing weakness in the hind extremities. This symptom was followed by the retraction of the head and paroxysm of violent convulsion; finally by death which resulted 40 minutes after injection.

3. *Chloroform soluble portion.* A portion of the chloroform extract was washed with ether and dried. 0.32 g. of the dried material were treated with 32 cc. of water, the insoluble matter removed by filtration and 2 cc. of the solution representing 0.02 g. of the extract were injected subcutaneously into a rat weighing 270 g. One hour after injection it showed weakness. After two hours diarrhea was observed. After 10 hours the rat had recovered completely.

4. *Volatile oil.* 2.6 g. of the volatile oil were emulsified by shaking vigorously with 2 cc. of water and half of the emulsion was injected subcutaneously into a white rat weighing 260 g. before separation into oil and water had taken place. Muscular weakness, espe-

cially in the legs was observed 2 hours after injection. The animal had recovered completely after 4 hours.

5. *Aqueous residue from steam distillation.* 1 cc. of this liquid injected hypodermically into a white rat of 280 grams caused weakness and quietness in the animal which, however, recovered after 20 hours.

The effect of heat on the toxic principle. 1.00 gram of the ethereal extract was triturated with hot water for three successive times until the aqueous solution no longer became colored. The aqueous solution was filtered to remove the insoluble matter and the filtrate boiled gently for one hour. The final solution was made up to 10 cc. and 1 cc. of this solution was injected hypodermically into a rat weighing 250 g. Twenty minutes after the injection the animal lay down showing weakness in the extremities and 28 minutes later paroxysm of violent convulsion in the opisthotonus position started and continued until death. The interval between the time of injection and death was 50 minutes.

The effect of acid upon the toxic principle. 1.00 g. of the ethereal extract was treated thoroughly with water and the aqueous solution of about 30 cc. was acidified with 3.0 cc. of N/6 H_2SO_4 and boiled for 40 minutes; the loss by volume by boiling being made up by frequent additions of water. During the boiling an aromatic odor was very noticeable. Some black resinous substance was formed at the same time. After the mixture had boiled for 40 minutes it was allowed to cool and treated with $BaCO_3$ until neutral to litmus paper and the solution filtered. The aqueous filtrate thus obtained was diluted to 10 cc. and one-tenth of this quantity was injected hypodermically into a rat of 200 grams body weight. Thirty-six minutes after injection the animal showed distress, weakness, and slowing of respiration. Complete paralysis of the legs was shown by its lying down upon its side and this was followed by death. No convulsion whatever was observed. The interval between the time of injection and death was 66 minutes.

Test for alkaloids. The aqueous solution made from the ethereal extract was used to test for alkaloid. It gave precipitates with solutions of potassium mercuric iodide and of iodine in potassium iodide. As tannins also form precipitates with these reagents these reactions can not be considered as conclusive evidence of the presence of alkaloid. Certainty as to the presence of the latter was obtained by applying these reagents to aqueous solutions detanninized by means

of hide powder. While the aqueous infusion of pure hide powder which served as blank yielded no reactions the unknown solution gave distinct precipitates. The presence of alkaloid is, therefore, indicated.

Extraction of the ether-soluble portion with different solvents. The ether extract of the alcoholic extract, after the removal of the solvent, resembled an oleoresin. It was, therefore, first freed from oils by washing repeatedly with heptane and then extracted, by refluxing on a water bath, successively with chloroform and ethyl acetate. After the removal of the solvents, the chloroform soluble portion left a semi-solid residue with a greenish color, and the ethyl acetate extract formed a solid cake with some crystalline substance, probably a glucoside. These portions are designated as following:

A. Chloroform-soluble portion.

B. Ethyl acetate-soluble portion.

C. Resin (insoluble in both solvents).

Resin. The resin consisted of a brown powder, was insoluble in ether, water, ammonium bicarbonate, and sodium bicarbonate, partially soluble in sodium carbonate and soluble in sodium hydroxide. It was acid in character and dissolved freely in acetone and alcohol. The resin was precipitated when its alkaline solution was acidified, but the amount of the precipitate was only about 50 p.c. of the original material.

Test for toxic albuminose.[1] The solubility of the toxic principle in water and the precipitates caused by alkaloidal reagents suggested the possible presence of toxic albuminose. A portion of the ethereal extract was triturated with distilled water and filtered, the filtrate being detanninized and used for the following tests.

1. Boiling of the solution, which had been acidified with acetic acid, did not coagulate the solution.

2. No coagulation was observed on boiling the solution which had been acidified with nitric acid.

3. With concentrated HNO_3 toxic albuminose forms a white ring, which on heating changes to yellow. In its place a brown color, but no precipitate was observed.

4. A brown solution resulted on heating with concentrated sodium hydroxide with the subsequent addition of a few drops of $CuSO_4$ solution.

[1] *Trier, Chem. d. Pflanzenstoffe, Berlin,* 1924, p. 464; *Rosenthaler, Grundzuege d. chem. Pflanzenuntersuch., Berlin,* 1923, p. 23; *Mathews, Physiol. chem.,* 3d. ed., 1921, p. 928.

5. When boiled with concentrated KOH and lead acetate no precipitate was formed.

6. With Millon's reagent it produced a red coloration.

7. On the addition of two volumes of a saturated solution of ammonium sulphate to one volume of the aqueous solution, turbidity of the solution was observed.

Some of these reactions (Nos. 3, 6 and 7) show the possible presence of some proteins but since the substance failed to give a test for sulphur it may not be a toxic albuminoid since sulphur is supposed to be a characteristic element.

Test for tannins.[1] For this purpose the aqueous solution prepared from the ethereal extract was used.

1. The aqueous solution was distinctly acid to litmus paper.

2. With ferric chloride solution it produced a blue coloration which turned brown on the addition of sodium hydroxide.

3. It reduced Fehling's solution rapidly.

4. With $K_2Cr_2O_7$ solution a dark red color developed which changed immediately to a brown crystalline precipitate.

5. It caused precipitation with an aqueous solution of lead acetate.

6. With ammoniacal solution of $K_3Fe(CN)_6$ a red-brown color appeared.

7. With lime water it produced a white precipitate which turned rapidly to brown.

8. With gelatine solution a white curdy precipitate was formed.

9. As has already been stated this solution formed precipitates with alkaloidal reagents.

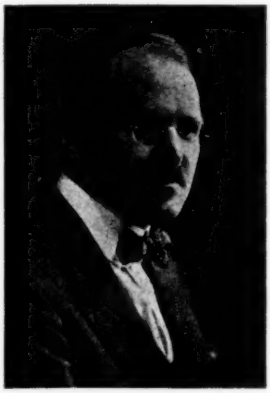
[1] Haas and Hill, *Introduction to Chem. of Plant Products* (1922), p. 93.

(*To be Continued*)

TWELVE POINTS IN U. S. P. POLICY

By E. Fullerton Cook, Chairman of the Committee of Revision of the United States Pharmacopœia

ONE HUNDRED and ten years of experience and earnest and honest planning for the health and welfare of this nation provide the background for the United States Pharmacopœia.



E. Fullerton Cook, Ph. M.

Happily, however, its age is no handicap, for the present Pharmacopœia is an aggressive, progressive and modern guide to medicine and pharmacy, fully in keeping with the spirit of up-to-date scientific progress.

As another decennial convention approaches there is rightly an intensified interest in every phase of the new revision and especially in its basic policies. Fortunately these policies are not fixed by immutable laws. In fact, most of them were established by no law but through the combined judgment and mutual acceptance of the various committees and are not even in print or writing.

For a more clear understanding of their character, a better opportunity to study them, and for their possible betterment, the chairman of the present committee is endeavoring to correlate the more important policies and explain their purpose and operation. While many other points might be brought under discussion in each division of the book, the following general considerations, basic in their applications, have been selected for this study:

1. Each New Pharmacopœia Should Represent the Best Medical and Pharmaceutical Knowledge of Its Day

In studying the life and words of Dr. Lyman Spalding, to whom almost alone we are indebted for the establishment of our National Pharmacopœia in 1820, the present chairman has been strongly impressed by his unselfish spirit and purpose. Dr. Spalding embodied this in the preface to the first U. S. P. when he wrote:

"It is the object of a Pharmacopœia to select from among substances which possess medicinal power, those, the utility of which is most fully established and best understood; and to form from them preparations and compositions, in which their powers may be exerted to the greatest advantage.

"The value of a Pharmacopœia depends upon the fidelity with which it conforms to the best state of medical knowledge of the day. Its usefulness depends upon the sanction it receives from the medical community and the public; and the extent to which it governs the language and practice of those for whose use it is intended."

The chairman was recently asked whether he advocates a small Pharmacopœia, and his reply then and today is that he is not concerned over the size of the Pharmacopœia, but only that it shall represent fully and completely and accurately the best medical and pharmaceutical knowledge of this our scientific and progressive age. Let it be large if we have the knowledge to justify it.

2. The First Requisite as a Guide to U. S. P. Admission is "Therapeutic Usefulness" or "Pharmaceutical Necessity"

These were the words adopted by the 1920 convention in determining the scope policy for the Tenth Revision. The committees are bound by this program in which therapeutic value and not *use* is clearly set forth as the deciding factor for admission, but the valuable drug must be sufficiently used to justify recognition.

In determining whether a therapeutic agent is useful we must depend upon the experts best qualified to judge the known facts.

3. The Committee of Revision Directed That Physicians Shall Decide Therapeutic Usefulness; Pharmacists Shall Decide Pharmaceutical Necessity

A calm survey of the facts will help many to develop their own judgment on this policy which was adopted by the Committee of Revision by a vote of 33 to 16 (1 not voting) after a thorough discussion in personal conference at Washington and later in the official circulars.

Let us follow the sequence of events:

The Pharmacopœia was founded by physicians and was under their exclusive control up to 1850. In 1850 the physicians invited pharmacists to co-operate because of splendid pharmaceutical help given voluntarily by pharmacists during the 1840 revision.

In the Ninth Revision (1910-1920) the vote of the Scope Sub-Committee was for the first time subjected to review by the larger committee (the Executive Committee), upon which physicians were in the minority, only five out of sixteen having an M. D. degree.

This action so incensed the physicians of the country that the Ninth Revision of the Pharmacopœia was largely discredited as an authority by the medical colleges and journals, and in the 1920 convention the chairman of the Revision Committee, Charles H. LaWall, who succeeded Chairman Remington when the latter died, made the following specific recommendation when discussing the weakness of a policy which required every member of the committee to vote on technical questions upon which they were not informed.

Chairman LaWall said:[1]

> "I believe it would be well for the convention at this time to give some very careful thought to this subject and to issue binding instructions to the incoming committee covering this very important phase of the work. For example, it certainly is exclusively the province of the medical members of the Revision Committee to decide what substances should be officially included for remedial purposes, and this list, after having been decided upon by the physicians, should not be subject to review or alteration by pharmacists and chemists. On the other hand, when the list of official remedial agents has once been clearly outlined, it should be the province and privilege of the pharmacists and chemists to decide upon such additions and inclusions of materials used as ingredients as will make it possible and practicable to prepare the medicine of proper uniformity, quality, and potency. These are the basic and fundamental prerogatives, and a workable plan should be devised to maintain their integrity."

This recommendation was referred by the convention to a committee consisting of Professors Wortley F. Rudd and J. A. Koch, who reported back to the convention as follows:[2]

> "The second matter has to do with the manner of arriving at decisions in matters of detail by the Committee of Revision, the chairman stating the belief that the convention should issue binding instructions to the incoming Committee of Revision covering this very important phase of the work. It has been the consistent policy heretofore not to hamper the Committee of Revision in its work by binding instructions of any kind and your committee

[1] Abstract of Proceedings, U. S. P. Convention, 1920, p. 69.
[2] Abstract of Proceedings, U. S. P. Convention, 1920, p. 87.

believes that it would be unwise to change the policy. The Committee of Revision should be left free, and should have full authority to deal with these questions to serve the end in view."

This recommendation was adopted by the convention and became a mandate to the chairman of the Committee of Revision and to the Committee of Revision. Note that there is no recorded opposition to this policy expressed by any member of the convention.

The adoption of a policy on this point was now squarely up to the Committee of Revision and was brought before the Committee for discussion by Dr. H. C. Wood, who requested that the General Committee define the status and relation of the Sub-Committee on Scope.[3] The first discussion was at Washington in the conference of the committee immediately following the convention. After "voluminous discussion," the following motions offered by George M. Beringer, a practicing pharmacist, were adopted, the first by a vote of 22 to 8, the second unanimously.

Mr. Beringer's motions were:

"In questions concerning the inclusion of substances of therapeutic usefulness in the Pharmacopœia the entire body of physicians on the Committee of Revision shall have the deciding vote.

"In all questions regarding the inclusion of substances of pharmaceutical necessity the entire body of pharmacists on the Committee of Revision have the deciding vote."

As all members had not been able to attend this meeting of the committee, on request of the chairman immediately declared the entire question open for reconsideration and asked for discussion and a new vote, all by mail.

The meeting at Washington was held on May 12, 1920, the minutes were mailed to all members on May 22d, the question opened for rediscussion on July 2d, the discussion published and a new vote called on July 17th, and the result of the final vote announced on July 31st, when 33 members voted in favor of the Beringer motions, 16 were opposed, and 1 did not vote.

Those who discussed this policy when it was before the committee a second time were Messrs. Dohme, Dye, Eldred, Fantus, Francis, Havenhill, Houghton, Jordan, Kelly, Kraemer, McCoy, Newcomb, Nitardy. Sollmann, Stitt and Wood.[4]

[3] See U. S. P. X Official Circulars, p. 7.

[4] See the Official Circulars of the Committee of Revision, pp. 73 to 79, pp. 130 to 137.

Those who voted in favor of this policy and gave the responsibility to the physicians alone to decide the admission of therapeutically active substances were: Messrs. Alsberg, Anderson, Arny, Barbour, Bastedo, Beringer, Bradley, Christian, Clark, Craig, DuMez. Edmunds, Fantus, Fussell, Gathercoal, Hamburger, Hatcher, Havenhill, Hodge, Hunt, LaWall, Leonard, McCoy, Nitardy, Pittenger, Rosengarten, Rowntree, Schneider, Seltzer, Sollmann, Stitt, Wood and Zeigler.

Those who opposed this policy were Messrs. Caspari, Cully, Dohme, Dye, Eldred, Francis, Houghton, Johnson, Jordan, Kelly, Kraemer, Murray, Newcomb, Richtmann, Ruddiman and Scoville. Dr. Diner did not vote.

Here was again a clear mandate to the chairman which he was called upon to administer. It is a remarkable fact that in a nation-wide campaign the chairman is charged with the responsibility for this policy with which he is in sympathy, but which he never proposed, never even discussed before the committee and which was approved by the General Committee by an overwhelming majority and placed in his hands to administer.

Evidently a fact brought to the attention of the committee in the original discussion by Dr. Sollmann is forgotten. He wrote:[5]

> "The real question is then: Who shall decide whether the therapeutic usefulness of a drug is such as to entitle it to admission to the Pharmacopœia? Who are the logical judges of this strictly therapeutic question, the physicians or the pharmacists?
>
> "The pharmacists doubtless have much information on this subject; there is every opportunity in the Beringer plan to make that information effective, but should the pharmacists be the final arbiters of a strictly medical question?
>
> "This would be the effect of leaving the decision either to the General Committee or to the Executive Committee; for it was planned by all parties that the pharmacists should predominate greatly on both committees. This plan received the hearty support of the medical delegates because they felt assured that there would be no serious question about leaving the therapeutic subjects to the judgment of the medical members, and therefore felt safe in furthering the election of a majority of pharmacists on both committees."

[5] Official Circulars, U. S. P. X p. 134.

As to the qualifications of the physicians of the committee to decide the value of drugs, a qualification which is also being questioned, Dr. Wood in the original discussion said:[6]

> "The medical men on the Revision Committee were chosen by the physicians of the convention in a widely announced caucus, and it is fair to assume that they were regarded by the medical delegates as those best qualified to represent medical science upon the Revision Committee. Why should we assume that they are less competent or less sincere than those selected by the pharmaceutical delegates to the convention? There seems to be a fear in the minds of some that the medical men are not fit to be trusted to make a decision in a matter which is peculiarly the province of physicians.
>
> "Dr. Dohme objects to leaving these decisions to Subcommittee No. 1 on the ground that 'pharmacologists are usually men not in actual practice.' Of the medical members of the Sub-committee on Scope, ten are today engaged in the practice of medicine, some of whom have never performed a pharmacological experiment in their lives; four are laboratory pharmacologists, that is men who are not practicing physicians at present. I do not know what experience these latter gentlemen may have had in the past in clinical medicine, but when the clinical physicians can outvote the purely laboratory men more than two to one, it seems to me rather far-fetched to fear that the committee will be dominated by the pharmacologists."

4. U. S. P. Standards of Quality Insure Maximum of Efficiency and Minimum Cost

When the U. S. P. became the official standard under the Food and Drugs Act in 1906, it became necessary to fix exact degrees of purity for its drugs, chemicals and preparations where these could be provided.

Chairman Remington was greatly interested in this policy and suggested the term "Purity Rubric" to apply to the clause which fixed the minimum degree of purity required. He often said that the Pharmacopœia prevented no manufacturer from exceeding the U. S. P. purity requirement, and rather stimulated that effort, but at the same time it conserved the interests of the sick by not demanding 100 per cent. purity and the corresponding cost when those impurities were harmless. At the same time that the U. S. P. tests ignored harmless foreign substances such as moisture, if the chemical was still sensibly dry, a little soda in a potassium salt, a little cinchonine in a quinine

[6] See the Official Circulars, p. 136.

salt, etc., yet it rigidly excluded or limited dangerous foreign substances such as arsenic and lead.

This policy keeps up the quality of the medicines of the Pharmacopœia without making their cost needlessly high.

5. The Revision Committee is made up of Experts in All Related Fields

In the U. S. P., 1920 convention, when nominations were being made for members of the Committee of Revision, the question, "What policy is to govern the convention in the selecting of such members?" was asked, and it was clearly understood that the individual's personal qualifications for work on the committee were to be the basis of selection and not geographic location or other such irrelevant reasons.

Such a policy will always insure a creditable and up-to-date Pharmacopœia for the United States.

6. Chiefly Volunteer Work on the Committee of Revision

This policy has always prevailed, for there is no financial reward for the members except a modest salary for the chairman, a small honoraria for each member of committee at the close of the revision, and necessary clerical expenses.

Small amounts have been allowed several of the sub-committee chairmen for laboratory assistants on certain experiments, but the policy of volunteer work is well established.

In discussing this recently in relation to the revision of the British Pharmacopœia the chairman pointed out that over a period of many years the Pharmacopœia has been able to command the interest and assistance of the most able men in medicine and pharmacy who were glad to contribute their experience and time to this philanthropic service. The help of such men could not have been secured by pay and the amount available for a few salaries, if all work had been on that basis, would have attracted other types of workers to the detriment of the Pharmacopœia.

7. Opportunity is Always Given Every Member to Discuss Every Question and See the Other Members' Opinions Before a Vote is Called

This has been a fixed policy of revision and has proven very satisfactory. When a question is placed before the committee, all members are invited to discuss it. Ample time is given for a reply (never

less than two weeks and often four weeks) before the discussion is copied in full in the official circulars, and a vote called.

Again two weeks is allowed for the return of the vote when the names of each and how they vote is published to the entire committee. The chairman has never heard a compliant from the working of this policy.

8. Maximum of General Publicity Concerning All Decisions Before Printing the U. S. P.

In the U. S. P. IX and again in the U. S. P. X the policy was followed of publishing in the pharmaceutical press an announcement of all important changes proposed for the new Pharmacopœia by the Committee of Revision and inviting comments or criticisms from any one who was interested. This policy also applied to all proposed deletions and new admissions.

All comments received by the chairman were published in full in the official circulars and considered in the final make-up of manuscript.

In the U. S. P. X, when the book had reached page proof this was sent for reading and criticism to about 200 selected experts in every field of the revision.

This policy increased the general interest in the revision, assisted the committee in correcting possible errors, and insured a much more acceptable Pharmacopœia.

9. Harmonious Cooperation Was a Notable Feature of the U. S. P. X Revision

Each group of experts worked in their special field throughout the revision and contributed their quota toward the finished revision. All members discussed and gracefully accepted the majority decision on all general questions. Over two hundred additional experts were elected as auxiliary members of sub-committees, and received all sub-committee bulletins and the privilege of discussion, but without vote.

In addition the Government organization, including the Hygienic Laboratory, the laboratories of the Bureau of Chemistry, the Bureau of Standards and the Prohibition Enforcement Division and also the Army and Navy Laboratories associated with offices of the Surgeon-General and many college, private, and manufacturers' laboratories combined in a remarkable illustration of harmonious co-operation toward a common goal.

10. A Convention and Committee of Technical Experts

Technical experts in therapeutics, pharmacy, chemistry, pharmacology, botany, pharmacognosy, serology, nomenclature and other related sciences, here gather on a common plane for an unselfish undertaking in the interest of public health. It is not duplicated by any other country in the world.

11. A New Convention and a New Pharmacopœia Every Ten Years

We owe this policy to the wisdom and foresight of Dr. Lyman Spalding, who suggested and established it at the first convention in 1820.

It has just been adopted as the policy for Great Britain, although they propose to adopt the fifth year of each decade for the start of a new revision. This period has proven satisfactory to most users of the book, as it gives ample time for adjustment between revisions, does not upset standards too frequently and provides ample time to develop and try new remedies and new technical methods.

12. A Policy of Independent Research

The Pharmacopœia Committee has, from time to time, undertaken independent studies of some of its problems by financing researches in private or other laboratories, but until recently this has been intermittent and no fixed policy.

In the current revision the chairman and the Executive Committee, under the authority of the by-laws of the convention, have adopted a definite policy for research and eight or ten such studies are under way, through the modest grants established by the Board of Trustees. As was recently announced, the Board of Trustees also recommends to the next convention the setting aside, as a memorial to Chairman Remington, of an initial amount of twenty thousand dollars the income of which is to be available for research on Pharmacopœial problems.

NOTES ON TESTS FOR METHANOL

By Henry Leffmann and Charles C. Pines

THE DETECTION of methanol has become of much importance of recent years on account of its use in crude form as a denaturant and its commercial production in high purity at a moderate price, the latter condition rendering it liable to be substituted for ethyl alcohol, a very dangerous practice. Our attention has been specially drawn to the question of the tests used for the detection of methanol in the presence of ethanol, by noting the procedure prescribed in the current (6th, 1926) edition of the *Deutsches Arzneibuch* and comparing this with the procedure directed in U. S. P. X. In the issue of this JOURNAL for April last, the German method was unfavorably criticised, attention being particularly called to the tedious routine for carrying out the oxidation by permanganate. Other minor objections were noted.

The criticism attracted the attention of Dr. R. Brieger, of the staff of the *Pharmazeutische Zeitung,* who kindly sent an explanatory letter and a clipping from that journal (1926, #96) being an article by H. Matthes, in which one phase of the procedure is deprecated, namely the use of guaiacol dissolved in strong sulphuric acid. Matthes substitutes potassium guaiacolsulphonate in equivalent amount. Runge about the same date had expressed disapproval of the reagent, suggesting guaiacolsulphonic acid, but it seems likely that a solution of guaiacol in strong sulphuric acid would produce some sulphonic acid promptly. It will be noted that both these criticisms were published shortly after the appearance of the German work. The reagent directed in the D. A. is 20 mg. of guaiacol dissolved in 10 cc. of strong sulphuric acid. Matthes recommends 40 mg. of the sulphonate on acount of the much higher molecular weight, more than double that of guaiacol. It seems better to use much more.

We have experimented with the process as suggested by Matthes and find it delicate. With careful attention to details, formaldehyde may be detected in very small amount and acetaldehyde does not simulate it. It is important that the sulphonate is in complete solution and the substances at room temperature. The colorless solution obtained in the U. S. P. process after the addition of the dilute sulphuric acid will give a satisfactory, though faint reaction with the

sulphonate solution, if methanol was present in the sample. A few drops of the colorless liquid should be placed on the reagent, and the rest tested with the fuchsin-sulphurous acid.

Matthes states that the test as modified will detect 1 part of formaldehyde in 6000. This is about equivalent to 0.6 cc. to the U. S. gallon. The German work directs that 10 cc. of the sample should be distilled, collecting 2 cc. 1 cc. is reserved for detection of acetone, and the other for methanol. This procedure will give a strong alcohol, and hence the German process prescribes 1 gram of permanganate for oxidation. The U. S. P. process requires the sample to be diluted so as to contain but about 5 per cent. of alcohol, and 5 cc. of this to be used. A small amount of permanganate is sufficient for oxidation. The use of the permanganate in dilute solution is much more satisfactory than the D. A. method (adding very small portions of powder at intervals). This is a serious objection to the German method, and in view of the fact as we noted above that the oxidation as obtained by U. S. P. method gives enough formaldehyde to react distinctly with Matthes' reagent, the use of dilute permanganate solution in small amount seems to be entirely safe.

LaWall, to whose comprehensive examination of the literature and extensive experimentation the present process is due, found that in ordinary application the delicacy is about 1 in 500. This is sufficient for the routine work in connection with control of lawful and unlawful traffic in alcoholic liquors. By distilling 10 cc. of the sample, collecting 1 cc. a delicacy of 1 in 10,000 may be reached, beyond which it is of course not necessary to go.

The U. S. P. X process has been extensively used and has proved satisfactory, but LaWall found that glycerol which is a not infrequent ingredient of factitious liquors, will simulate exactly the methanol reaction. Distillation of the sample would seem to be the method to eliminate this error, but Dr. Hepburn informed us that Dr. T. M. Price, of the Department of Agriculture, had found that enough of the glycerol or some decomposition product thereof will pass over to simulate methanol with the fuchsin-sulphurous test. Potassium guaiacolsulphonate, however, gives no reaction with the glycerol product. In these tests we have used a solution containing 100 mg. of the sulphonate in 10 cc. of sulphuric acid, which is more than double the amount recommended by Matthes.

The German work recommends that the color test should be made on a watch glass resting on a white surface, but Matthes states

that procelain dishes are much more satisfactory. We have found this to be the case, but have also found that small porcelain crucibles are still more suitable. We have used those holding about 10 cc. designated by dealers as No. 00. If the colorless liquid obtained after addition of sulphuric acid in the U. S. P. test is distilled, collecting about half the original volume, a still more marked color can be obtained with Matthes' reagent.

Summary

The substitution of potassium guaiacolsulphonate for guaiacol is a marked improvement in the test for formaldehyde.

The test is a useful check on the fuchsin-sulphurous acid test, serving especially to distinguish the glycerol from the methanol reaction, preliminary distillation seeming not to be entirely safe for such purpose.

The U. S. P. process for oxidation is accurate, delicate and convenient. The tedious piecemeal addition of powdered permanganate as directed by the *Deutsches Arzneibuch* is unnecessary.

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SOLUBILITY OF SODIUM SALICYLATE IN ALCOHOL [1]

By W. Schnellbach

THE SOLUBILITY of sodium salicylate in alcohol as stated in the U. S. P. X was recently questioned. The U. S. P. gives the solubility as "1 gm. of sodium salicylate in 9.2 cc. of alcohol at 25 degrees C." The following experiments were made to settle the question.

A mixture of U. S. P. alcohol and an excess of U. S. P. powdered sodium salicylate was placed in a Pyrex test tube, tightly stoppered and constantly shaken by a mechanical stirring apparatus in a water bath at a temperature of 25 degrees ± 0.05 degrees C. After

[1] This investigation was conducted under the direction of Dr. George D. Rosengarten in the Laboratory of the Philadelphia College of Pharmacy and Science under a grant provided by the Board of Trustees of the U. S. Pharmacopœial Convention.

four days a portion of the solution was withdrawn and quickly filtered under precautions which avoided the volatilisation of the solvent. An adequate portion of the solution was accurately weighed in a weighing bottle, the alcohol evaporated and the residue finally dried at 100 degree C. to constant weight.[2] After eleven days of continued agitation two additional samples of the solution were withdrawn and dried in the same manner. All three analyses yielded the same result as indicated in the table below.

Time of Shaking in Days	Gm. of Solution Taken for Analysis	Gm. of Residue Obtained	Gm. of Sodium Salicylate Present in 100 Gm. of Solution
4	5.1580	0.5890	11.74
11	2.2708	0.2666	11.74
11	1.8938	0.2160	11.74

Conclusion: 11.74 gm. of sodium salicylate are present in 100 gm. of an alcohol solution saturated at 25 degrees C. Therefore: 1 gm. of sodium salicylate is soluble in 9.33 cc. (= 7.52 gm.) of U. S. P. alcohol[3] at 25 degrees C.

This result is very close to the U. S. P. X statement.

DETERMINATION OF THE WATER CONTENT OF STRYCHNINE SULPHATE[1]

By W. Schnellbach

THE STRYCHNINE sulphate of the U. S. P. contains five molecules of water of crystallization and it is required that it should not lose more than 11 per cent. of its weight on drying at 100 degrees C. The theoretical percentage of water of crystallization in strychnine sulphate pentahydrate is 10.57. The U. S. P. therefore permits a small amount of "moisture" water.

[2] The original sodium salicylate lost on drying at 100° C. less than 0.1%, an amount which may be safely ignored.

[3] The specific gravity of the alcohol used in this determination was 0.8176 $\frac{15.5^\circ}{15.5^\circ}$ corresponding to a density of 0.8083 $\frac{25^\circ}{4^\circ}$

[1] This investigation was conducted under the direction of Dr. George D. Rosengarten in the Laboratory of the Philadelphia College of Pharmacy and Science under a grant provided by the Board of Trustees of the U. S. Pharmacopœial Convention.

The claim was made by a strychnine manufacturer that their product contains 11.5 per cent. of water corresponding to five and one-half molecules of water of crystallization. A check of the water content of the commercial strychnine sulphate was therefore desirable.

First the literature was consulted. *Beilstein* mentions two modifications of crystallized strychnine sulphate: a pentahydrate crystallizing in monoclinic prisms, and a hexahydrate crystallizing in tetragonal form, mostly in square octahedrons. Beilstein refers to the investigation of Rammelsberg,[2] who obtained from a hot solution thin prisms containing 10.82 per cent. of water. From a cold saturated solution which was allowed to evaporate slowly at room temperature he obtained octahedrons, containing 12.77 per cent. of water. Both results are close to the theoretical values of the pentahydrate and the hexahydrate respectively, as may be seen from the following table:

Modification	Theoretical Percentage	% H_2O Found
Pentahydrate	10.51	10.82
Hexahydrate	12.36	12.77

Samples of strychnine sulphate U. S. P. were procured from two sources. They were designated *A* and *B*. Sample *A* was from the regular stock of a well known chemical manufacturer. Sample *B* was furnished by the firm which claimed their product contains five and one-half molecules of water of crystallization.

Sample *A* consisted of thin, perfectly colorless needles of about 5 mm. average length. Some of the crystals were slightly effloresced. Sample *B* was presented by two specimens: crystals (designated *B* I) and powder (designated *B* II). The crystals, *B* I, consisted of long, thick needles. Crystals 10 mm. long and more were quite numerous. They were slightly discolored as compared with sample *A*. Small crystals of cubic shape and slightly yellow color were also observed in this sample. They were either loose or clinging to the large crystals. These (the small cubic shaped crystals) could easily be selected and were separately analyzed. The powder, *B* II, was perfectly white and no particular crystalline form could be recognized under the microscope. Later another sample of strychnine sulphate

[2] *Berichte der Deutschen Chemischen Gesellschaft* 14, 1231 (1881).

(*B* III) was procured from the same firm. The crystals were colorless and slightly effloresced. Crystals of square shape could not be observed.

Sample *A*, which was provided in a larger quantity, was used for many crystallization experiments under varying conditions. The original sample is designated *A* I. *A* II was prepared by recrystallizing a portion of *A* I in the following manner. About 4 gm. of the sample were heated with 60 cc. of water and some decolorizing carbon and the solution hot-filtered into an Erlenmeyer flask, which was rapidly cooled under the running tap water with constant agitation. The first crystals appeared when the solution had reached a temperature of 27 degrees C. When the temperature fell to 25 degrees C. it remained constant until the excess of dissolved strychnine sulphate had separated. The crystalline powder so obtained was collected on a disc of filter paper in a Gooch crucible and the adhering solution removed by suction.[3] The product was dried over sulphuric acid for about two hours and finally kept in a desiccator, containing anhydrous strychnine sulphate, until costant weight was obtained. The crystalline powder, when observed under the microscope, appeared as square plates indicating the crystals to be of tetragonal form.

A III was obtained by allowing a cold saturated solution to evaporate spontaneously at room temperature in a beaker covered with filter paper. This solution as well as the following were treated with decolorizing carbon. Plate like crystals appeared in a few days and grew to almost cubic form.[4]

A IV was crystallized at 56 degrees ± 1 degree C. It yielded granular crystalline masses of no particular form.

A V was crystallized at 44 degrees ± 1 degree C. The final product consisted of crystalline masses which included considerable amounts of mother liquor which could be seen under the microscope. The analysis also yielded a higher percentage of water than was expected.

The series of *A* IV to *A* IX was made to determine the limiting crystallization temperature of the two modifications. The crystal-

[3] In many cases a high speed centrifuge was employed for this purpose. The filter, containing the damp crystals, was placed in a weighing bottle on top of a pledget of cotton and centrifuged.

[4] The tetragonal crystals are mostly of tabular development, showing very prominent basal pinacoid, in combination with prism, consequently the hexahydrate always appears in (fairly thick) square plates.

lizations were made in a suction flask under vacuum, the flask being immersed in a water bath. The temperature in the flask as well as that of the water bath were constantly observed during the crystallization, and they could be kept constant with ± 1 degree C. The temperature of the water bath had to be from 10 degrees to 15 degrees C. higher than that desired for the crystallization. All these crystallizations yielded small but loose crystals. They were collected and dried in the manner already described. The temperature of the crystallization and the appearance of the product under the microscope are shown in table *A*.

Analytical

The original samples *A* and *B* and all products obtained by recrystallization were analyzed by determining the water and the sulphuric acid. For the estimation of water a special apparatus [5] was used which allowed the determination not only of the loss of weight but also the actual amount of water expelled on drying. For the sulphuric acid the method of Winkler and Schulek [6] was employed.

Theoretical percentage of H_2O and H_2SO_4 in strychnine sulphate pentahydrate and hexahydrate.

Modification	% H_2O	% H_2SO_4
Pentahydrate	10.51	11.45
Hexahydrate	12.36	11.21

[5] Described subsequently.

[6] *Zeitschrift für angewandte Chemie* 33, I, 59-60, 159-160, 161-163 (1917). See for description in details the paper on solubilities in the August issue of the *Journal of the American Pharmaceutical Association*, 1929.

TABLE A.—RESULTS OF ANALYSES OF STRYCHNINE SULPHATE
(SAMPLES A)

Sample		Form	% of H_2O Found	Corresponding % of H_2SO_4 Calculated [9]	% of H_2SO_4 Found	Number Mol. H_2O
A I	Original commercial sample	Needles about 5 mm. length	10.63 [7] 10.69 [7] 10.73 (10.83) [8]	11.42	11.48	5
A II	Crystallized at 26°±1° C. from supersat. solution	Crystalline powder square plates under the microscope	12.05 (12.07)	11.25	11.15	5.8
A III	Crystallized at room temp. from saturated solution	Square plates or cubes 3-5 mm. edge length	12.49 (12.51) 12.39 (12.30)	11.20	11.21 11.20	6
A IV	Crystallized at 56°±1° C. in open beaker	Granular masses	11.78 (11.81)	11.35	11.36	5.4
A V	Crystallized at 44°±1° C. in open beaker	Irregular crystalline masses occluding mother liquor	12.42 (1204) 12.30 (12.41)	11.22	11.24	5.9
A VI	Crystallized at 53°±1° C. under vacuum	Crystalline powder, needles under the microscope	10.89 (10.89)	11.40	.....	5.2
A VII	Crystallized at 46°±1° C. under vacuum	Crystalline powder, needles under the microscope	10.56 (10.44)	11.45	11.45	5
A VIII	Crystallized at 40°±1° C. under vacuum	Crystalline powder, square plates and a very few needles under the microscope	12.31 (12.36) 12.33 (12.40)	11.22	.....	6
A IX	Crystallized at 39°±1° C. under vacuum	Crystalline powder, square plates under the microscope	12.26 (12.36)	11.22	11.21	6

[7] Dried in drying oven at 120° C.

TABLE B.—RESULTS OF ANALYSES OF STRYCHNINE SULPHATE

(SAMPLES B)

Sample		Form	% of H_2O Found	Corresponding % of H_2SO_4 Calculated[9]	% of H_2SO_4 Found	Number Mol. H_2O
B I	Original sample	Needles and square plates	11.31 (11.34)[8]	11.35	11.25	5.8
B II	Original sample	Powder	11.49 (11.51)	11.3	11.35	5.4
B III	Original sample	Needles of 5 mm. average length	11.24 (11.15)	11.35	11.31	5.6
B I	Separate Analyses of prisms and square plates found in sample B I	Needles 10 mm. length	.....	.....	11.38	5.3
		Square plates, 2 mm. edge length	.....	.....	11.05	>6.0

[8] The data in brackets are derived from the increase of weight of the absorption apparatus.

[9] These data represent values based upon the average H_2O found. They were read of a graph representing the percentage of water and sulphuric acid. From five to six molecules of water of crystallization were plotted along the abscissa and the percentages along the ordinate. (See Fig. 2.) The percentage of water corresponding to the percentage of sulphuric acid found is not indicated in the table, for the percentage of water alters 7.8 times as fast as the percentage of sulphuric acid, as may be seen from the ratio of the differential derivatives of the equations representing the percentage of water and sulphuric acid:

$$\frac{d(\%H_2O)}{d(\%H_2SO_4)} = \frac{-(\text{strychnine sulph.})}{(\text{sulphuric acid})} = -7.8$$

That means that a small variation in the sulphuric acid determination causes a large deviation in corresponding percentage of water.

The water content of the sample *A* was in accordance with the U. S. P. requirement. In the three samples *B* it varied between 11 and 12 per cent., confirming the claim of the manufacturer. The analyses of the sample *B* I is of particular interest. This sample consisted, as already mentioned, of needles and small square shaped crystals. The latter form, suspected as representing the hexahydrate, was separated and analyzed. About 0.15 gm. were obtained from about 7 gm. of the material. The sulphuric acid found corresponded to somewhat more than six molecules of water of crystallization. The deviation from the theoretical value may be due to the small quantity of crystals analyzed thus introducing the possibility of a larger analytical error. The analysis of some of the largest needles present in the sample *B* I, yielded a result corresponding to somewhat more than five molecules of water of crystallization. This was probably due to the small tetragonal crystals (hexahydrate) which under the miscroscope were observed to cling to the needles (pentahydrate).

Summary

The determination of the water content in commercial crystallized strychnine indicated that it may vary and will sometimes exceed the 11 per cent. allowed by the U. S. P. X.

On consulting the literature it was found that two crystalline modifications of strychnine sulphate, a pentahydrate (monoclinic) and a hexahydrate (tetragonal) have been definitely known since 1881.

One specimen of crystallized strychnine sulphate, claimed by the manufacturer to contain 11½ per cent. of water of crystallization (5½ molecules), was found to consist of a mixture of the two hydrates.

A series of crystallizations was made at different temperatures. In accordance with the statement, found in the literature,[10] they yielded the pentahydrate at temperatures above 40 degrees C. and the hexahydrate below this temperature.

In recrystallizing strychnine sulphate at various temperatures no form containing exactly five and one-half molecules of water of crystallization was found. Preparations with a water contents deviating from the theoretical values of the pentahydrate or the hexahydrate, are considered to be a mixture of the two hydrates.

[10] Groth, *Chemische Kristallographie* (W. Engelmann, Leipzig, 1919), Vol. V, page 971.

The apparatus used for the determination of the water in strychnine sulphate is shown in the accompanying sketch. The tared boat, *A*, weighed with the chemical to be examined, is placed in a glass tube, *B*, which is surrounded by a larger metal tube and through which steam, generated in the flask, *I*, is passed. A slow stream of air is conducted through the inner tube, *B*. The water escaping from the chemical in the boat is absorbed in the U-tubes, *D* and *E*.[11] These

Figure 1—This photograph shows Strychnine Sulphate, Pentahydrate and Hexahydrate (square plates) on the bottom of a beaker, natural size.

tubes were weighed before and after the completion of the experiment. The same absorbing agent was used in the entire absorbing

[11] After the first few experiments with calcium chloride as absorbent it was found much more convenient to use a potassium bulb containing sulphuric acid. In this case also sulphuric acid was used to dry the air before passing through the tube, B.

train and all the tubes were kept at the same temperature during the run of the experiment.

K is a constant-level device. A relatively wide tube, *a*, connects the boiler, *I*, with the water reservoir, *K*, furnishing the boiler with water as it boils off. The tube *a*, must be of fairly wide size so that steam or air is able to escape into the reservoir. The tubes, *b* and *c*, are provided to permit filling of the reservoir without disconnecting. To refill the apparatus the tube, *a*, is closed by a pinch cock, tube, *b*, is connected with the suction pump and tube, *c*, is lengthened and

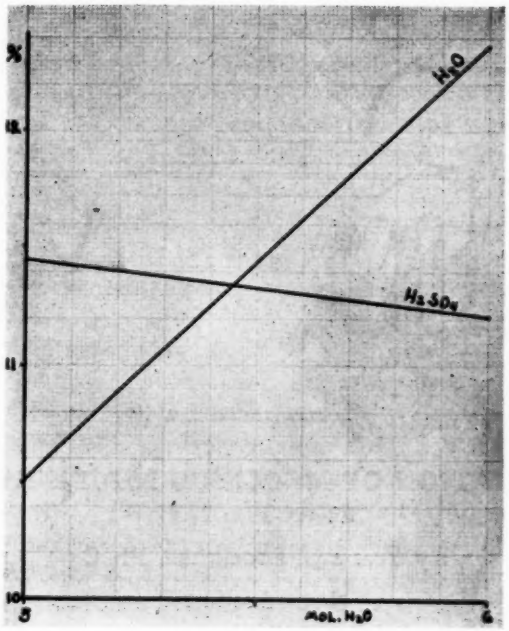
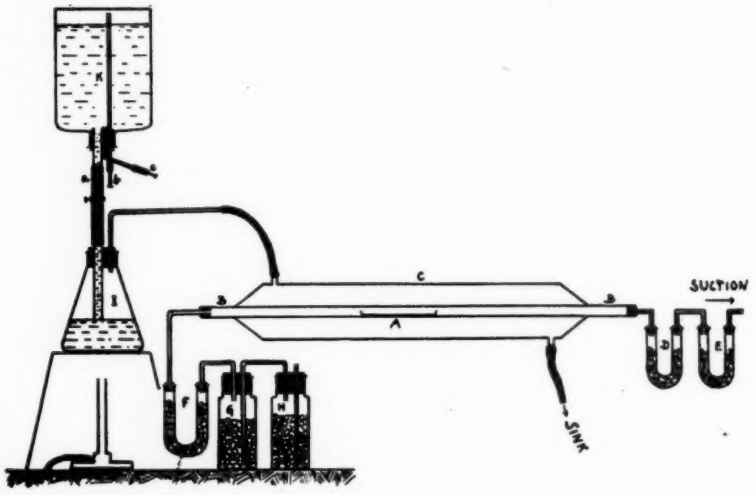


Figure 2

passed into a bottle of distilled water (the steam was condensed in a bottle after passing the heating tube, *C*, and used to refill the reservoir). The suction pump is then turned on and the water sucked into the reservoir, *K*. Both tubes, *b* and *c*, are closed again and the pinch cock opened. The refilling can easily be done during the run of an experiment.

In determining the absorbed water by this apparatus a more reliable result is obtained than by simply drying the chemical in a drying oven, especially in cases of chemicals which, if dehydrated, rapidly absorb moisture from the air and therefore do not permit an accurate determination of the loss of weight.



DETERMINATION OF MERCURIC IODIDE BY IODATE REACTIONS*

By Frank G. Brockman, Ph. C.

Introduction

OF THE various strictly chemical methods for the determination of the purity of mercuric iodide none is of sufficient reliability and simplicity to warrant its acceptance by the United States Pharmacopœial Revision Committee, with the result that the present method is an electrolytic one. With this in mind the following work

*An abstract of the thesis presented to the Faculty of the Philadelphia College of Pharmacy and Science as a partial fulfilment of the requirements for the degree of Bachelor of Science and representing an investigation conducted in the Analytical Chemistry Laboratory of the College.

was carried out in an attempt to develop a practical, routine method for the analysis of mercuric iodide, which would necessitate nothing other than ordinary apparatus.

1. Oxidation by Potassium Iodate

George S. Jamieson, in a compilation [1] of practical volumetric methods using potassium iodate as the volumetric reagent, gives a method for soluble iodides which consists in titrating the iodide directly in the presence of hydrochloric acid. The iodate first decomposes the iodide by the reaction:

$$5KI + KIO_3 + 6HCl = 6KCl + 3H_2O + 3I_2;$$

the reaction, in the presence of 12 per cent. or more of HCl, then proceeds as follows:

$$2I_2 + KIO_3 + 6HCl = KCl + 5ICl + 3H_2O.$$

Completion of the reaction is indicated by the discharge of the color of the liberated iodine imparted to chloroform added near the end of the reaction.

This method was applied to the insoluble mercuric iodide in the following manner:

Transfer a sample of about 0.5 gm., accurately weighed, of mercuric iodide to a 125 cc. glass stoppered bottle, add 20 cc. of hydrochloric acid (1.16) and about one-half the calculated volume of approximately fifth normal potassium iodate (i. e. for a 0.5 gm. sample add 13 cc.). Stopper the bottle and shake vigorously. Again add the volumetric solution but now more slowly, stopper and shake the bottle thoroughly after each addition, until the mercuric iodide has completely entered into solution. Up to this time about three-quarters of the necessary volume of the volumetric solution will have been required. Introduce five cc. of chloroform and continue titrating until the color imparted to the chloroform by the liberated iodine is just discharged.

The results of some determinations carried out by this method are tabulated below:

$$1 \text{ cc. } KIO_3 \text{ v. s.} = 0.009367 \text{ gm. } KIO_3$$
$$= 0.01989 \text{ " } HgI_2.$$

[1] Volumetric Iodate Methods, Geo. S. Jamieson, The Chemical Catalog Co., Inc.

Weight HgI_2	KIO_3 v.s.	Purity HgI_2
0.5012 gm.	25.08 cc.	99.53%
0.4998 "	25.04 "	99.65 "
0.3005 "	15.10 "	99.95 "
0.4012 "	20.10 "	99.65 "
0.4038 "	20.24 "	99.69 "
0.4017 "	20.00 "	99.03 "
0.5001 "	25.00 "	99.43 "
0.5124 "	25.66 "	99.60 "
0.4390 "	21.96 "	99.50 "
0.4916 "	24.73 "	100.05 "
0.5353 "	26.81 "	99.62 "
0.3597 "	18.24 "	100.80 "
0.5726 "	28.60 "	99.35 "
0.4795 "	24.04 "	99.72 "
0.3446 "	17.20 "	99.28 "
0.3485 "	17.51 "	99.93 "
0.3681 "	18.42 "	99.53 "

Average purity 99.62 per cent.,

Greatest deviations from this average + 1.2, —0.6.

It is the author's conviction that the error of weighing is one of the primary causes of the variable results of this method. The difficult solubility of the mercuric iodide also made the process tedious but the ready solubility of mercuric iodide in potassium cyanide solution, which was called to the attention of the author by Prof. Frank X. Moerk, was considered worthy of investigation.

The results follow of 18 titrations of 10 cc. portions of a solution containing 7.2500 gms. of mercuric iodide and 3.68 gms. of potassium cyanide in 200 cc. The process was in accord with the previous directions.

1 cc. KIO_3 v.s. = 0.010607 gm. KIO_3
= 0.022523 " HgI_2.

Weight HgI_2	KIO_3 v.s.	Purity HgI_2
0.3625 gm.	16.02 cc.	99.54%
" "	16.00 "	99.41 "
" "	16.05 "	99.72 "
" "	16.00 "	99.41 "
" "	15.97 "	99.22 "
" "	16.01 "	99.47 "
" "	16.00 "	99.41 "
" "	15.98 "	99.29 "
" "	15.97 "	99.22 "
" "	16.00 "	99.41 "
" "	16.00 "	99.41 "
" "	16.02 "	99.54 "
" "	16.00 "	99.41 "
" "	15.99 "	99.35 "
" "	16.00 "	99.41 "
" "	16.00 "	99.41 "
" "	16.05 "	99.72 "
" "	16.00 "	99.41 "

Average purity 99.41 per cent.

Greatest deviation from this average +0.3 per cent., —0.2 per cent.

In order to show that the potassium cyanide did not react with any of the iodate, two solutions, one of 3.68 gms. of potassium cyanide in 200 cc. and the other of 5.2000 gms. of potassium iodide in 200 cc. were prepared. Three ten cc. portions of the iodide solution were titrated with potassium iodate, factor 0.01063 gm. KIO_3, by the same method used for the mercuric iodide; and then three more, but with ten cc. of the potassium cyanide solution added to each ten cc. of the potassium iodide solution, before titration. There was no effect to be noted due to the presence of the potassium cyanide as is to be seen from the results:

KI Without KCN.

Weight KI	KIO_3 v.s.	Purity KI
0.2600 gm.	15.73 cc.	99.75%
" "	15.70 "	99.57 "
" "	15.70 "	99.57 "

KI with KCN.

Weight KI	KIO_3 v.s.	Purity KI
0.2600 gm.	15.71 cc.	99.63%
" "	15.70 "	99.57 "
" "	15.70 "	99.57 "

The results of this method were much more concordant than those of the first and formed the basis of the following procedure:

2. Modified KIO_3 Method

Dry about 5 gms. of mercuric iodide to constant weight over sulphuric acid, weigh accurately, transfer to a 100 cc. volumetric flask, add 50 cc. of a 5 per cent. solution of potassium cyanide and 40 cc. of distilled water, dissolve by gentle agitation, dilute to accurately 100 cc. and mix. Titrate a 10 cc. aliquot portion of the solution contained in a 125 cc. glass stoppered bottle, with fifth normal potassium iodate, adding about half the necessary volume at once (about 13 cc.). Then add 20 cc. of hydrochloric acid and 5 cc. of chloroform. Continue titrating, stoppering and shaking the bottle thoroughly after each addition of volumetric solution, until the color imparted to the chloroform by the liberated iodine is just discharged. Each cc. of fifth normal potassium iodate contains 0.01070 gm. KIO_3 and corresponds to 0.02272 gm. of HgI_2.

The following tabulation contains the results of twelve titrations of different complete operations carried out according to the above method.

1 cc. KIO_3 v.s. = 0.010627 gm. KIO_3
= 0.02257 " HgI_2.

Weight HgI_2	KIO_3 v.s.	Purity HgI_2
0.5000 gm.	22.00 cc.	99.31%
" "	22.02 "	99.40 "
" "	22.05 "	99.53 "
" "	22.06 "	99.58 "
" "	22.05 "	99.53 "
" "	22.05 "	99.53 "
" "	22.05 "	99.53 "
" "	22.10 "	99.76 "
" "	22.11 "	99.80 "
" "	22.12 "	99.85 "
" "	22.05 "	99.53 "
" "	22.00 "	99.31 "

Average purity 99.55 per cent.

Greatest deviation from this average +0.3 per cent., —0.2 per cent.

CACAO BUTTER

By David Wilbur Horn and Arthur Osol [1]

CHOCOLATE COATINGS, for confectionery, cakes, etc., are distributed in the trade with little respect to geographical factors, although climate and season affect coatings considerably. Genuine chocolate coatings for low temperature products (such as ice cream bricks) offer serious problems. Such considerations some years ago led one of us to the preparation on a small scale of an oleine and a stearine from cacao butter. It is obvious that in modifying coatings an autogenous oleine or stearine would be preferable to a similar extraneous product such as one from the coconut. The oleine

[1] Many of the results in this paper are from work submitted by Arthur Osol to the Philadelphia College of Pharmacy and Science in partial fulfilment of the requirements for the degree of M. S.

and stearine from cacao butter were later prepared on a manufacturing scale.

The object of the present paper is primarily to present the experimental results obtained in the laboratory in comparison of this commercial-scale oleine and stearine with cacao butter. At the same time a comparison was made with cacao butter from liquor "Dutched" in the nib.

Refractive Index

Our measurements were made on the Abbe refractometer with heated prisms. This instrument is stated by Zeiss to give readings "with a degree of exactness approaching to within about two units of the fourth decimal."

In the literature of the trade the scale readings on the Zeiss butyro-refractometer at 40 degrees C. are usually given. Some of these statements along with the corresponding refractive indices are given.

TABLE 1.

Trade Authority [2]	Limiting Scale Readings	Corresponding Refractive Indices
Zipperer	46.0 to 47.8	1.4565 to 1.4578
Whymper	46.0 to 47.0	1.4565 to 1.4573
Bolton & Revis	46.0 to 47.5	1.4565 to 1.4576
Bolton & Revis, "Typical Specimen"	46.7	1.4571
Allen 4th Ed. p. 702	46.0 to 48.0	1.4565 to 1.4580

In order to be able to form an opinion as to the probable value of the refractive index of *run-of-mill* cacao butter known not to be sophisticated, measurements were made of butters produced under widely varying conditions. The results are given in Table 2. Samples were taken from different presses of different types operating upon the same and different liquors at such times as to include first-

[2] Zipperer, *Die Schokoladen-Fabrikation*, 3d Ed., p. 60. Whymper, *Cocoa and Chocolate, Chemistry and Manufacture*, p. 256. Bolton & Revis, Fatty Foods, *Practical Examination*, p. 165. *Allen's Commercial Organic Analysis*, 4th Ed., VI, p. 702.

runnings, middle portions and tailings from the presses, from liquors made from one kind of bean and from many kinds blended, in winter and in summer, at brief intervals and after long intervals, and from tanks containing large accumulations of butters collected from genuine liquors of many kinds. Finally cacao butters from various factories after varying lengths of time were examined. These results all appear in Table 2.

TABLE 2.

Date	Time in Min.	Press	Liquor	No. of Kinds of Nibs in Liquor	R. I. at 40° C.	Location
1/26	0	6	1	4	1.4571	
	90	5	1	4	1.4571	
	105	6	1	4	1.4572	
	112	3	2	3	1.4571	Start
	120	3	2	3	1.4571	Intermediate
	127	3	2	3	1.4571	"
	140	4	3	2	1.4573	Middle
	148	4	3	2	1.4570	Near end
	155	4	3	2	1.4571	Tailings
	163	6	2	3	1.4571	
	170	3	4	1	1.4571	
	178	2	2	3	1.4570	
	187	7	4	1	1.4572	
	190	Tank	C.[3]		1.4571	
	197	1	3	2	1.4572	
2/2	0	6	5	6	1.4571	
	5	4	4	1	1.4571	
2/9	0	4	6	4	1.4570	
	7	5	6	4	1.4571	
	14	2	5	6	1.4570	
	21	3	5	6	1.4571	
	28	6	5	6	1.4570	
2/16	0	1	7	4	1.4571	
	13	2	7	4	1.4571	
	18	5	6	4	1.4571	

[3] "C" means *Composite, i. e.*, made up of a mixture of cacao butters from six or more presses working on liquors No. 1 to No. 4, inclusive.

Date	Time in Min.	Press	No. of Kinds of Nibs in Liquor	Liquor	R. I. at 40° C.	Location
	26	3	6	4	1.4572	
	37	3	6	4	1.4571	
2/26	0	5	8	4	1.4571	
	7	1	8	4	1.4571	
	18	2	8	4	1.4571	
	24	3	8	4	1.4570	
	32	5	8	4	1.4571	
	39	6	8	4	1.4571	
	53	Tank	8 & 7	6	1.4571	
	63	Tank	7	4	1.4570	
6/10	0	3	6	4	1.4572	
	7	5	6	4	1.4572	
	15	2	8	4	1.4572	
	25	2	8	4	1.4573	

Factory		Age of Sample	Refractive Index
No. 1	Domestic	4 years	1.4573
No. 2	Foreign	3 years	1.4573
No. 3	Domestic	1 year	1.4572
No. 4	Foreign	1 year	1.4570

We believe these measurements justify the conclusion that *run-of-mill* cacao butter (if pure) may reasonably be expected to show a refractive index at 40 degreec C. of 1.4571 ± .0002. This agrees with Revis and Bolton's figure for their "Typical Specimen," cited in Table 1.

The four products which are primarily the subject of this paper showed refractive indices as follows:

TABLE 3.

Pure cacao butter	1.4572 at 40 degrees C.
Commercial oleine of cacao butter	1.4579 " " " "
Commercial stearine of cacao butter	1.4580 " " " "
Dutched cacao butter	1.4578 " " " "

It is evident that all four products fall within the trade limits set forth in Table 1, but that the oleine, stearine and Dutched butter run higher in refractive index than does "typical" cacao butter.

Surface Tension

The surface tension at the surface between the melted substance and air was determined with a du Noüy Tensiometer by the ring method. The differences in scale reading upon the four different products were so slight as to leave doubt as to whether or not they were significant.

Table 4 sets forth the results. They were obtained at 40 degrees C., maintained pretty constantly in the fat by placing the fat in a quartz dish mounted upon an "Electric Incubator for the Microscopic Stage"—a thermostated device that was placed upon the adjustable "table" of the du Noüy apparatus. Between experiments, the platinum ring was washed in petroleum ether and then heated red hot in the Bunsen flame.

TABLE 4.

Article	Scale Reading	Surface Tension in Dynes per Centimeter
Cacao butter	49.6	35.5
Oleine	49.1	35.2
Stearine	48.8	34.9
Dutched cacao butter	49.7	35.7

The greatest difference in surface tension among these products is only 0.9 dyne per centimeter. We are not aware that the surface tension of cacao butter has been measured before.

Viscosity

When we attempted to determine the viscosities of these four products at 80 degrees C. in the Sayboldt Universal viscosimeter, there was always more or less clogging of the outlet and satisfactory results were not possible. In a Stormer viscosimeter it was possible to make a comparison of these four products. The results are given in Table 5. In column 5 of this table we also give the cane sugar solution that we found to give the same result at 25 degrees C., as

the cocoa butter at 80 degrees C., in the Stormer viscosimeter. The exact values were gotten by interpolation along a short curve obtained by plotting seconds required for 100 revolutions of the drum of the viscosimeter in 38, 40 and 42 per cent. by weight cane sugar solutions,[4]

TABLE 5.

Article	Secs. Required for 100 Revolutions at 80° C. (Average)	No. of Determinations Averaged	Average Deviation (Secs.)	Sucrose Sol. with Same Running Time (at 25° C.)
Cacao butter	21.8	8	±0.2	39.50%
Oleine	22.7	11	±0.2	40.18%
Stearine	22.0	11	±0.2	39.65%
Dutch cacao butter	21.1	11	±0.3	38.97%

Melting Point

Only by the use of the Wiley method was it possible to get concordant results upon the melting points of these products.[5] Table 6 sets forth the results of several examinations and the average melting point found in the case of each product. The determinations were all made on small discs that had previously been kept in a cool place more than twenty-four hours.

TABLE 6.

Product	Det. No. 1	Det. No. 2	Det. No. 3	Average Melting Pt. Degrees C.
Cacao butter	33.4	33.0	33.2	33.2
Oleine	31.5	31.7	....	31.6
Stearine	34.7	34.7	34.5	34.6
Dutched cacao butter	33.2	33.5	33.2	33.3

[4] See "Standard Substances for the Calibration of Viscometers," Bingham & Jackson, U. S. Bureau of Standards Scientific Paper, No. 298.

[5] The capillary tube method given for cocoa butter in the Official Methods of Analysis of the Association of Official Agricultural Chemists gave results that were very difficult to use. There was as great a difference as 6° found by this method between the temperatures of incipient fusion and of complete fusion. See Methods of Analysis of A. O. A. C., 2d Ed., pages 347 and 284.

These measurements of melting point bring out clearly the characteristic differences usually noted between a fat and its oleine and stearine.

Specific Gravity

The specific gravities of the melted products were determined by filling the pycnometer at 99 degrees C. with the fat and at 15 degrees C. with distilled water. The capacity of the pycnometer was approximately 10 cc. Table 7 sets forth the average results obtained.

TABLE 7.

Article	Average Wt. of Fat in Pycnometer	Specific Gravity $\frac{99°}{15°}$
Cacao butter	8.5830	0.8572
Oleine	8.5827	0.8572
Stearine	8.5845	0.8574
Dutched cacao butter	8.5868	0.8576

No characteristic differences appear in these specific gravities.

Transition Point

The four products were subjected to a study as follows: The melted fat was placed in a Dewar test tube, which was held firmly in the center of a bath of water and ice. The fat was stirred constantly with a thermometer and when its temperature had fallen to 33 degrees C. or thereabout, the readings of the thermometer every minute were written down. The results were then plotted, the temperatures vertically and the time horizontally. In general the form of the resulting graph is that of the root-sign of algebra $\sqrt{}$. The liquids gradually cool until they are undercooled as much as 5 to 10 degrees; finally crystallization sets in accompanied by a gradual rise in temperature. This rise continues to a maximum, which maximum is maintained quite exactly to within 0.1 degree for a period (in our experiments) of from 8 to 20 minutes. This temperature we have called the *transition point* of the product. Table 8 sets forth the transition points thus obtained.

TABLE 8.

Product	Transition Point Set No. 1	Set No. 2	Average
Cacao butter	29.4	29.3	29.3
Oleine	27.9	27.8	27.8
Stearine	28.8	28.9	28.9
Dutched cacao butter	30.0	30.0	30.0

In order to make clear the procedure, we give the results and the graph in one such determination. Table 9 is an abbreviated table of results, omissions having been made whenever such omissions did not change the path of the graph.

TABLE 9.

Time	Temp.	Time	Temp.	Time	Temp.
0	32.5	32	29.1	46	30.0
6	28.9	34	29.6	47	30.0
12	26.0	35	29.7	48	30.0
18	23.8	36	29.8	49	30.0
19	23.5	37	29.9	50	30.0
20	24.0			51	30.0
21	24.7	38	30.0	52	30.0
22	26.3	39	30.0	53	30.0
23	27.0	40	30.0	54	29.9
24	27.3	41	30.0	58	29.7
26	27.9	42	30.0	63	29.3
		43	30.0		
28	28.3	44	30.0	70	28.8
30	28.8	45	30.0	75	28.4

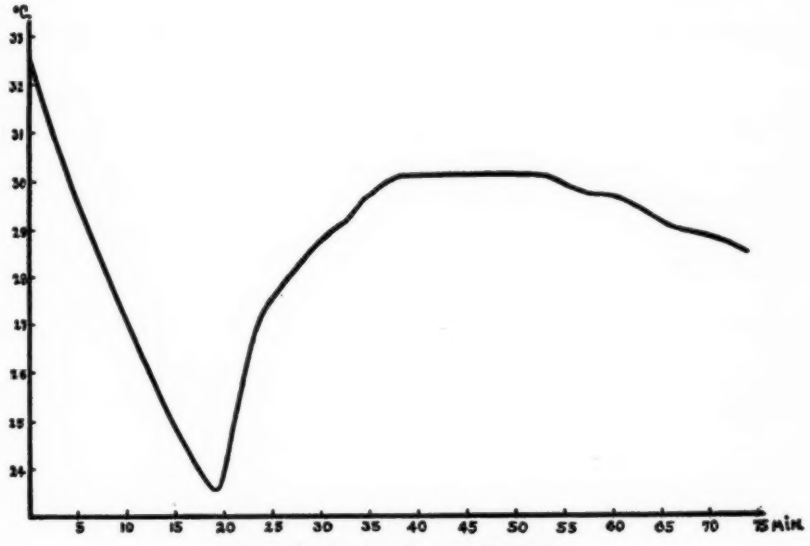
The transition points seem about as satisfactory as the melting points by the Wiley method for bringing out the difference among these four products.

Acidity

The acidity stated as milligrams of KOH required to neutralize the acid in 1 gram of fat was determined in duplicate on all four products. Table 10 sets forth the results.

TABLE 10.

Product	Weight Taken	Cubic Centimeters NaOH Required	Acidity	Mean Acidity
Cacao butter	3.4232	1.50	2.49	
" "	2.6081	1.10	2.40	2.44
Oleine	3.1660	1.80	3.24	
"	3.2694	1.95	3.39	3.31
Stearine	2.1973	1.00	2.59	
"	2.6103	1.20	2.62	2.60
Dutched cacao butter	2.1511	1.05	2.78	
" " "	3.1074	1.55	2.84	2.81



"DUTCHED" COCOA BUTTER

The acidity value brings out a distinct difference between the oleine and stearine, but the stearine differs in acidity from cacao butter less than the Dutched cacao butter differs from cacao butter. To what extent these acidity values may involve "rancidity" we are however unable to say.

Liquid Fatty Acids

The "lead salt ether" method was used, applied however only to the oleine and stearine. Table 11 gives the results.

TABLE 11.

Product	Weight of Fat Taken	Weight of Acids Found	Per Cent. Acids
Oleine	5.1495	1.9020	36.9
Stearine	5.0741	1.9206	37.8

The results are of no assistance in distinguishing these products.

Saponification Number and Unsaponifiable Matter

These values were gotten by the usual procedure, giving results which would scarcely enable one to differentiate the four products.

TABLE 12.

Product	Weight Taken	cc. H_2SO_4 for Excess NaOH	Saponification Number	Average S. N.	Weight of Residue	Per Cent. of Unsaponifiable Matter
Cacao Butter	1.8168	13.20	194.68			
" "	2,1818	15.85	194.64	194.66	0.0157	0.76
Oleine	2.2166	16.10	194.61			
"	2.2366	16.25	194.66	194.63		
"	3.3206				0.0299	0.90
Stearine	2.0725	15.00	193.92			
"	2.5350	18.30	193.42	193.67		
"	2.2594				0.0209	0.93
Dutched C. B.	2.9278	21.32	195.01		0.0143	0.90
" "	1.5878	11.50	194.03	194.52	0.0264	0.90

Iodine Number

The results of these determinations (made with Hanus' solution) enable one to distinguish the oleine and stearine analytically from the cacao butters.

TABLE 13.

Product	Weight Taken	Iodine Number Found	Average Iodine Number
Cacao butter	1.2183	37.74	
" "	1.1919	37.72	37.73
Oleine	0.3507	40.87	
"	0.7195	41.51	
"	0.4220	41.27	
"	0.5422	40.45	41.02
Stearine	0.6984	38.60	
"	0.6000	38.66	
"	0.3049	38.90	
"	0.5519	38.62	38.69
Dutched cacao butter	0.9912	36.95	
" " "	1.9116	37.09	37.02

Summary

We have conducted comparative tests upon commercial samples of cacao butter, cacao butter oleine, cacao butter stearine, and cacao butter from "Dutched" nibs.

Although these four products are different, the differences lie within the range of experimental error in our determinations of specific gravity of saponification number, of unsaponifiable residue and of liquid fatty acids by the lead salt ether method.

The differences lie not far outside the range of experimental error in our determinations of refractive index at 40 degrees C., of surface tension at 40 degrees C., of viscosity (Stormer) at 80 degrees C.

Distinct indications of differences are brought out in our determinations of iodine number (Hanus), of melting point (Wiley) and of "transition point" and possibly also, of acidity.

We are not aware that "transition point" of fats and oils have heretofore been determined; we find the procedure simple and regard it as well worth trying in other similar cases.

Our experiments show some change in the cacao butter in the process of "Dutching," > *i. e.*, heating > with mixtures of carbonates or hydroxides of the alkalis and alkaline earths, so that this cacao butter is not exactly the same as pure cacao butter.

MEDICAL AND PHARMACEUTICAL NOTES

NEW BLUE FOOD DYE APPROVED BY DEPARTMENT OF AGRICULTURE—An additional food dye has been approved for inclusion in the list of colors that will be certified by the United States Department of Agriculture, according to a recent announcement by the Food, Drug and Insecticide Administration.

This color, which will be known as Brilliant Blue FCF and which has been known chemically for many years, has been tested both chemically and physiologically and found to be harmless to health and otherwise suitable for food use, according to the Federal food officials.

CHEMICALS NO HELP IN KEEPING CUT FLOWERS—Placing cut flowers in a bath of aspirin or other chemicals in an effort to prolong their life is useless according to this authority. Experiments conducted at the Boyce Thompson Institute for Plant Research here showed that none of fifty different chemicals, used in the hope of increasing the life of cut flowers, were noticeably effective. Potassium permanganate did prevent decay of the stems of phlox and asters but it did not make the floral parts last any longer. Other chemicals in some cases actually caused injury to the flowers.

Low temperatures were a great help in keeping roses, carnations, and coreopsis, but the cold did not greatly benefit either cosmos or dahlias. Humidity is also an important factor in keeping cut flowers. Carnations kept two to three times as long in an atmosphere which was nearly saturated with moisture.

AVERAGE LENGTH OF LIFE DECLINING—In spite of the efforts of physicians and public health workers, and notwithstanding the proud boasts of some of them, we are not living as long as men of earlier generations and the average length of life is declining, Prof. C. H. Forsyth of Dartmouth College has found. For the American adult, the odds are at present heavily against his living as long as his father or grandfather, Prof. Forsyth declares in a report in the forthcoming issue of Science. The average American adult is in the midst of a

decidedly losing fight which he cannot win until he applies himself energetically to being superior to his environment.

Prof. Forsyth takes issue "with those who are so elated with results obtained in their own immediate fields leading to significant reductions not only in certain death rates but also in the prevalence of certain diseases that they feel justified in predicting marvelous increases in the average length of the whole of life in the no great future."

"Most of these optimistic authorities have failed to appreciate that practically all these results have been attained in children's diseases and that little or no attention has been given to the situation at ages beyond the prime of life," stated Prof. Forsyth.

The expectation of life at advanced ages, that is, the number of years that a man of fifty, for example, may expect to live, is definitely declining, Prof. Forsyth found from his exhaustive study of many mortality tables and population statistics.

"The expectation of life from age forty-five or fifty on is the lowest of which we have any record—far lower than it was even forty years ago—and it is still going down, not up," Prof. Forsyth declared. "With all the improvement in the world at the early ages, the present downward trend at the advanced ages, if unchecked, will continue to dominate and produce a greater and greater net decline in the average length of life.—*Science Service.*

BOOK REVIEWS

BOTANY, by William J. Robbins and Harold W. Rickett. Van Nostrand Co., New York, 1929. 535 pages—382 illustrations, 101 book references. Net price $3.75.

In twenty-seven chapters we find an interesting discussion of cells and tissues, their contents, growth and function, of origin and meaning of life, relations, energy of representative groups of lower and higher plant life, their vegetative and sexual life cycle inheritance, evolution and distribution.

In spite of the "many excellent textbooks available on botany allied subjects," as the authors admit, they have prepared the elaborated course of lectures, given at the University of Missouri, in an

attempt "to present the fundamental biological principles rather than to lay the foundation for professional botany, and to give "a correct idea of the true nature of the aim of science its methods of work, and the value and limitations of its results."

To illustrate the author's treatment we quote from the chapters of reactions of plants. "Teleology is a very human point of view and we do many things with purpose; and we assume that the things which a plant or animal does are also caused by purposes . . . It must be emphasized that science cannot deny the possibility that plants have wills and purposes, and that they govern its life, or that there is some all-knowing Power directing their activities. Teleology may represent, for all we know, the truth; but it is unscientific nevertheless, because it assumes things for which there is as yet no evidence in the sense of observable or demonstratable facts. Therefore we must avoid it in Biology—the scientific consideration of life. We must give as reasons for structures and function only known causes; and we must be prepared, when we cannot find the cause, frankly to admit our ignorance—and to go on looking for one."

Curiously we find no references to lignin, so characteristic of all woody tissue, of hemicellulose, mucilage and the cellose of sieve tubes. We also feel with regret, that bio-chemistry and bio-physics have not been given more place as they form such an integral part of modern biological science.

Appended is a questionnaire of over 500 questions for review and discussion which will prove helpful to the student who all too frequently is at a loss to formulate his own questions and to determine the extent of his understanding and knowledge.

The book will prove suggestive to the teacher of botany or biology—and be welcomed by students of plant life.

ARNO VIEHOEVER.

THE PHARMACEUTICAL RECIPE BOOK.

Over eighteen years have elapsed since the Committee on the Recipe Book of the American Pharmaceutical Association was appointed to consider the advisability of the Association publishing a druggists' recipe book. While the committee labored long to do the work allotted to it, it also labored well and faithfully to bring into being a book that reflects great credit to the Association as well as to the committee itself.

The first edition of the Pharmaceutical Recipe Book embodies a list of formulas of preparations not published in any other official publication. That there was a keen need for such a book goes without saying. Scattered throughout the literature of medicine and pharmacy were many valuable remedial preparations, for which pharmacists were constantly receiving demands, without having access to any reliable source for supplying these demands. Now all this is altered. As time goes on, this book will, we believe, become almost as necessary to the practice of pharmacy as the National Formulary.

The comprehensiveness of the matter embodied in the book will undoubtedly appeal to all types of pharmacists. Retail pharmacists, hospital pharmacists, and laboratory workers will find much to aid and stimulate them to endeavor in their particular branches of pharmacuetical work. We believe that, as time goes on, the value to pharmacy in general, of having an authentic reference book, of matter of interest to the different branches of pharmacy, will be more clearly perceived and appreciated by the profession.

Pharmacy today is confronted with a spirit of competition which is sharper than ever, and made doubly so because it comes from many directions. How to meet that competition and survive is the problem of the average pharmacist. Of course, he is a professional man, trained along scientific lines, but no matter how well trained, he is bound to fail if he does not know how to capitalize his professional training by sound business sense. Indeed, business itself is a science. No professional man, no matter how great his ability, be he clergyman, physician, lawyer, etc., can bring complete service to those he would serve, if he neglects to study how best to direct notice to his wares and to his ability.

In the Recipe Book there is material galore, with which the pharmacist can direct the attention of the medical profession toward himself. The average physician is always on the lookout for prescriptions and new ways of prescribing the well-known remedies. In that part of the book, devoted to hospital formulas, the pharmacist will find much that should interest the physicians whom he serves, provided he has learned how to give information without giving offense.

The physician takes kindly to any prescription or formula that claims the distinction of having originated in some hospital of standing and reputation. He knows, and the writer would emphasize this point, that such formulas are the result of long, practical experience.

Twelve of the great hospitals of the country are represented in this collection of hospital formulas.

Another department of the Recipe Book that should be of value to the pharmacist, in his endeavor to serve the medical profession, is that devoted to laboratory reagents. Many physicians do some laboratory work, and who should be better qualified to sell them the necessary reagents and stains to carry out clinical tests than the neighboring pharmacist. The chapter on laboratory reagents contains much that the pharmacist could profitably utilize.

Under the heading, "Pharmaceutical Formulas," one hundred and ninety pages embrace a variety of formulas that the pharmacist could, with perfect propriety, bring to the attention of his medical friends. Ten pages are devoted to ampuls, formulas for various solutions of drugs that are best administered in this manner, and a brief but clear description of the technic involved in the sterilization of ampuls. If the retail pharmacist can convince his medical clientele that he is equipped and able to prepare extemporaneous solutions in ampul dosage form, he will, undoubtedly, find a ready response. Hypodermic medication is becoming increasingly popular; the Recipe Book helps to meet this demand.

Under the heading, "Surgical Dressings," information, pertaining to the preparation of medicated cotton and medicated gauze, is presented briefly but clearly. While it may be true that the average retailer rarely has occasion to prepare these, such things being generally supplied by the large manufacturers of surgical supplies, he should know how such surgical material is prepared and have ready access to information on the subject.

To the retail pharmacist who wishes to cater to the "cosmetic urge," the chapter on cosmetics presents many inviting opportunities for profit. Never before in the history of the world has the weaker sex been so interested in the things that will enhance beauty.

In certain localities, veterinary remedies are needed and who, other than the pharmacist, should or could be better equipped by training and experience to take care of such needs? The same can be said in reference to the needs of photography. The material in the Recipe Book covering photographic work is most comprehensive.

It has always been a cause of wonder to the writer as to why the pharmacist fails to go after the flavoring extract business. The profit is more than good. And if the pharmacist would call to the

attention of his housewife customers the fact that he not only supplies all kinds of flavoring extracts, but makes all that he supplies as well, he surely would add to his prestige. It should not be hard to convince such customers that flavoring extracts from the "drug store" are far superior to those from the grocery store. The Recipe Book, then, gives information on the subject of flavoring extracts that certainly should enable the pharmacist to absorb a large share of this business.

Part Nine of this really useful book contains, under the title, "Technical and Miscellaneous Formulas," a variety of recipes on such subjects as Cements, Fumigators and Deodorants, Inks, Insecticides (how best to exterminate the Japanese beetle), Fly Exterminators, Laundry Accessories, Moth Preparations, Paints and Lacquers, Furniture Polishes, Ebony Stain for Wood, Fertilizers for Potted Plants, Anti-Freeze Mixtures and so-forth.

In a number of states the law requires that factories and workshops be equipped with "First Aid" outfits. The Recipe Book describes in detail what such an outfit should contain. The kinds of instruments, the different drugs, and dressings are all mentioned.

A careful perusal of the Recipe Book will convince anyone that the pharmacist who neglects to add this book to his reference library is most certainly cheating himself.

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ENGLER-PRANTL. DIE NATUERLICHEN PFLANZENFAMILIEN (The Natural Plant-Families)—2nd Edition, 1928, 447 illustrations.

In this new volume of the remarkable well-known series, Lindemann discusses the peridineæ (dinoflagellates), Karsten the diatomes, and, Jahn the slime molds (myxomycetes).

Lindemann first mentions an elaborate list of references, then the characteristics, the vegetative organs, the biology, occurrence, general position and relationship and concludes with the statements that fossil (silicified) forms occur in certain firestones, that they and the diatoms represent the main food of the sea and that certain forms may grow so abundantly as to cause pollution and death of other animals. Surprisingly, no statement is made of their occurrence and

usefulness and their clearing of polluted waters, such as originates from sewage-disposal plants.

Karsten, before treating in detail the main representatives, cites the literature, general characteristics, occurrence, morphology, physiology, their migration with sea currents, and the usefulness of the fossil forms as diatomaceous earth, of the living forms as fish food.

Jahn, discussing the slime molds, enumerates literature, characteristics, occurrence, morphology, physiology, distribution, history, and the harm that may occur to germinating plants in seed beds, to wet meadow grasses and moist hay, due to the development of common slime molds.

The volume is another testimonial to the scientific workmanship exhibited in this series.

ARNO VIEHOEVER.